```
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR 7):2


* * * * * * * * * *  Welcome to STN International  * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS  3  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS  4  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS  5  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS  6  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS  7  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS  8  JAN 29  PHAR reloaded with new search and display fields
 NEWS  9  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 10  FEB 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 11  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 12  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13  FEB 26  MEDLINE reloaded with enhancements
 NEWS 14  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 15  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 18  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19  MAR 16  CASREACT coverage extended
 NEWS 20  MAR 20  MARPAT now updated daily
 NEWS 21  MAR 22  LWPI reloaded
 NEWS 22  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS 23  APR 02  JICST-EPLUS removed from database clusters and STN
 NEWS 24  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25  APR 30  CHEMCATS enhanced with 1.2 million new records
 NEWS 26  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 27  APR 30  INPADOC replaced by INPADOCDB on STN
 NEWS 28  MAY 01  New CAS web site launched
 NEWS 29  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS 30  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS 31  MAY 21  BIOSIS reloaded and enhanced with archival data
 NEWS 32  MAY 21  TOXCENTER enhanced with BIOSIS reload
 NEWS 33  MAY 21  CA/CAplus enhanced with additional kind codes for German
                  patents
 NEWS 34  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                  patents

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
```



```
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:18:24 ON 30 MAY 2007

=> file reg
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:18:37 ON 30 MAY 2007
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STRUCTURE FILE UPDATES:   28 MAY 2007  HIGHEST RN 935999-19-2
DICTIONARY FILE UPDATES:  28 MAY 2007  HIGHEST RN 935999-19-2

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10.561754\clm14.str
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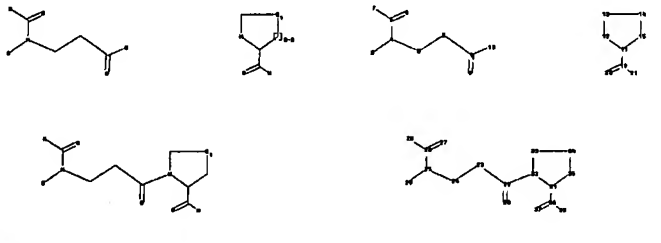

```
chain nodes :
1  2  3  4  5  6  7  8  9  10  19  20  21  22  23  24  25  26  27  28  29  30  36
37  38
ring nodes :
11  12  13  14  15  31  32  33  34  35
chain bonds :
1-2  1-9  1-10  2-3  3-4  4-5  4-8  5-6  5-7  11-19  19-20  19-21  22-23  22-30
22-32  23-24  24-25  25-26  25-29  26-27  26-28  31-36  36-37  36-38
ring bonds :
11-12  11-15  12-13  13-14  14-15  31-32  31-35  32-33  33-34  34-35
exact/norm bonds :
1-2  1-9  1-10  2-3  3-4  4-5  4-8  5-6  5-7  11-12  11-15  11-19  12-13  13-14
14-15  19-20  19-21  22-23  22-30  22-32  23-24  24-25  25-26  25-29  26-27  26-28  31-32  31-
35  31-36
32-33  33-34  34-35  36-37  36-38


G1:C,S

Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  19:CLASS  20:CLASS  21:CLASS  22:CLASS
23:CLASS
24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS  30:CLASS  31:Atom  32:Atom  33:Atom
34:Atom  35:Atom  36:CLASS  37:CLASS  38:CLASS
fragments assigned product role:
containing 22
fragments assigned reactant/reagent role:
containing 1
containing 11



L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
```



```
=> file casreact
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.45       0.66

FILE 'CASREACT' ENTERED AT 08:19:13 ON 30 MAY 2007
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FILE CONTENT:1840 - 27 May 2007 VOL 146 ISS 23

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*************************************************************
*                                                           *
*     CASREACT now has more than 12 million reactions       *
*                                                           *
*************************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 08:19:21 FILE 'CASREACT'
SCREENING COMPLETE -        0 REACTIONS TO VERIFY FROM        0 DOCUMENTS

100.0% DONE       0 VERIFIED       0 HIT RXNS                      0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:          0 TO        0
PROJECTED ANSWERS:                0 TO        0

L2            0 SEA SSS SAM L1 (      0 REACTIONS)

=> s l1 sss full
FULL SEARCH INITIATED 08:19:30 FILE 'CASREACT'
SCREENING COMPLETE -       14 REACTIONS TO VERIFY FROM        4 DOCUMENTS

100.0% DONE      14 VERIFIED       2 HIT RXNS                      1 DOCS
SEARCH TIME: 00.00.01

L3            1 SEA SSS FUL L1 (      2 REACTIONS)

=> d ibib abs hitstr
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
```

```
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number. SCAN
             must be entered on the same line as DISPLAY, e.g.,
             D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for
             all single-step reactions)
STD -------- BIB, IPC, and NCL

CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first
             hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
             CA reference information (SO, PY). (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction
             Summary for all hit reactions and fields containing
             hit terms
OCC -------- All hit fields and the number of occurrences of the
             hit terms in each field. Includes total number of
             HIT, PATH, SPATH reactions. Labels reactions that have
             incomplete verifications.
PATH ------- Reaction Map and Reaction Disgram for the "long
             path". Displays all hit reactions, except those
             whose steps are totally included within another hit
             reaction which is displayed
RX --------- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summaries (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short
             path". Displays all single step reactions which
             contain a hit substance. Also displays those
             multistep reactions that have a hit substance in both
             the first and last steps of the reaction, except for
             those hit reactions whose steps are totally included
             within another hit reaction which is displayed

To display a particular field or fields, enter the display field
codes. For a list of the display field codes, enter HELP DFIELDS
at an arrow prompt (=>). Examples of combinations include: D TI;
D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
```



```
as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
be used with the DISPLAY command to display the record for a specified
Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):end

=> d ibib abs hit


L3   ANSWER 1 OF 1  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         142:113909  CASREACT  Full-text
TITLE:                    Process for preparation of N-[oxidopyridinyl)
                          L-prolinamide derivatives
INVENTOR(S):              Slade, Joel; Vivelo, James Anthony; Chen, Guang-Pei;
                          Bajwa, Joginder Singh; Parker, David John
PATENT ASSIGNEE(S):       Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE:                   PCT Int. Appl., 34 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
     WO 2005000835     A1    20050106      WO 2004-EP6915   20040625
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     AU 2004251876     A1    20050106      AU 2004-251876   20040625
     CA 2530142        A1    20050106      CA 2004-2530142  20040625
     EP 1641778        A1    20060405      EP 2004-740324   20040625
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
     BR 2004011921     A     20060815      BR 2004-11921    20040625
     CN 1829710        A     20060906      CN 2004-80021438 20040625
     US 2007060753     A1    20070315      US 2005-561754   20051221
PRIORITY APPLN. INFO.:                    US 2003-482686P  20030626
                                          WO 2004-EP6915   20040625
OTHER SOURCE(S):          MARPAT 142:113909
GI
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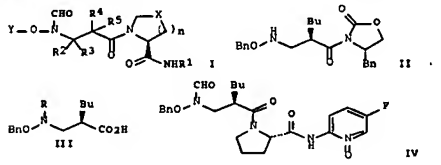
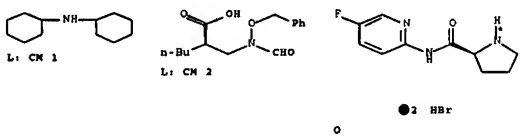


AB A process for the preparation of title compds. of formula I [Y = a OH protecting group; R1 =(hetero)aryl; R2-R5 = independently H or alkyl, or R2R3 and/or R4R5 = cycloalkyl; X = CH2, S, CH(OH), etc.; n = 0-3] is disclosed. For example, contacting II•TsOH with 1N Na2CO3 in EtOAc to move TsOH and oxidation by H2O2 gave III (R = H). Formylation of III with formic acetic anhydride gave III (R = CHO). Reaction of III with HBr salt of N-(5-fluoro-2-pyridinyl)-2-pyrrolidinecarboxamide, followed by oxidation , gave IV. Thus, the present invention provides a process producing the title compound, which are useful to prepare certain antibacterial N-formyl hydroxylamine compds. as peptide deformylase inhibitors.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(3) OF 10 ...L + O ===> P...



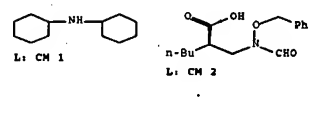

```
RX(3)      RCT  L 821774-93-0

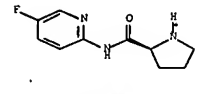
           STAGE(1)
             RGT  Q 77-92-9 Citric acid
             SOL  7732-18-5 Water, 141-78-6 AcOEt
             CON  SUBSTAGE(1) room temperature
                  SUBSTAGE(2) 10 minutes, room temperature

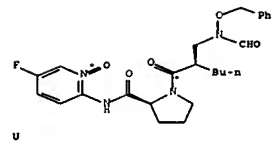
           STAGE(2)
             RCT  O 821774-95-2
             RGT  R 2592-95-2 1-Benzotriazolol, S 109-02-4
                  N-Methylmorpholine, T 25952-53-8 EDAP
             SOL  7732-18-5 Water
             CON  SUBSTAGE(1) room temperature
                  SUBSTAGE(2) room temperature -> 5 deg C
                  SUBSTAGE(3) room temperature
                  SUBSTAGE(4) overnight

           PRO  P 478913-92-7

RX(7) OF 10 COMPOSED OF RX(3), RX(4)
RX(7)      L + O ===> U
```







RX(3) RCT L 821774-93-0

STAGE(1)
RGT Q 77-92-9 Citric acid
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)
RCT O 821774-95-2
RGT R 2592-95-2 1-Benzotriazolol, S 109-02-4
N-Methylmorpholine, T 25952-53-8 EDAP
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 5 deg C
SUBSTAGE(3) room temperature
SUBSTAGE(4) overnight

PRO P 478913-92-7

RX(4) RCT P 478913-92-7
RGT V 109536-69-8 2-HO2CC6H4CO3H.Mg
PRO U 476913-93-8
SOL 108-21-4 Acetic acid, 1-methylethyl ester, 7732-18-5 Water
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 17 hours, room temperature
NTE workup

=> d cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	0.78	1.32
NETWORK CHARGES	0.12	0.24
SEARCH CHARGES	113.10	113.10
DISPLAY CHARGES	6.73	6.73
FULL ESTIMATED COST	120.73	121.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

IN FILE 'CASREACT' AT 08:20:14 ON 30 MAY 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	121.63	122.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

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STRUCTURE FILE UPDATES: 28 MAY 2007 HIGHEST RN 935999-19-2
DICTIONARY FILE UPDATES: 28 MAY 2007 HIGHEST RN 935999-19-2

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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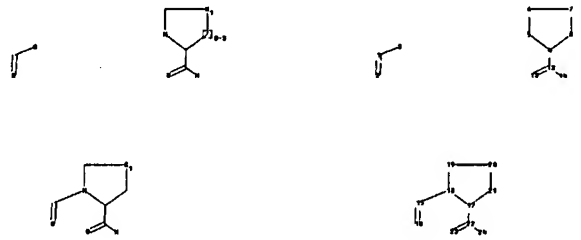
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10.561754\clm14 crop1.str



chain nodes :
1 2 3 12 13 14 15 16 22 23 24
ring nodes :
4 5 6 7 8 17 18 19 20 21
chain bonds :
1-3 1-2 4-12 12-13 12-14 15-18 15-16 17-22 22-23 22-24
ring bonds :
4-5 4-8 5-6 6-7 7-8 17-18 17-21 18-19 19-20 20-21
exact/norm bonds :
1-3 1-2 4-5 4-8 4-12 5-6 6-7 7-8 12-13 12-14 15-18 15-16 17-18 17-21
17-22 18-19 19-20 20-21 22-23 22-24

G1:C,S

Match level :
1:CLASS 2:CLASS 3:CLASS 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 12:CLASS 13:CLASS
14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:CLASS 23:CLASS
24:CLASS

fragments assigned product role:
containing 15
fragments assigned reactant/reagent role:
containing 1
containing 4

L4 STRUCTURE UPLOADED

=> d
L4 HAS NO ANSWERS
L4 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> file casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	122.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.73

FILE 'CASREACT' ENTERED AT 08:21:56 ON 30 MAY 2007
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FILE CONTENT:1840 - 27 May 2007 VOL 146 ISS 23

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
* *
* CASREACT now has more than 12 million reactions *
* *
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4
SAMPLE SEARCH INITIATED 08:21:59 FILE 'CASREACT'
SCREENING COMPLETE - 1557 REACTIONS TO VERIFY FROM 83 DOCUMENTS

100.0% DONE 1557 VERIFIED 930 HIT RXNS 50 DOCS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

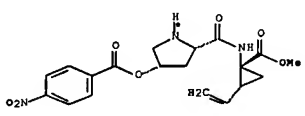
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 28776 TO 33504
PROJECTED ANSWERS: 899 TO 1901

L5 50 SEA SSS SAM L4 (930 REACTIONS)

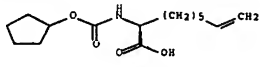
=> d ibib abs hit 1-10

L5 ANSWER 1 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:142133 CASREACT Full-text
TITLE: Epimerization Reaction of a Substituted Vinylcyclopropene Catalyzed by Ruthenium Carbenes: Mechanistic Analysis
AUTHOR(S): Zeng, Xingzhong; Wei, Xudong; Farina, Vittorio; Napolitano, Elio; Xu, Yibo; Zhang, Li; Haddad, Nizar; Yee, Nathan K.; Grinberg, Nelu; Shen, Sherry; Senanayake, Chris H.
CORPORATE SOURCE: Department of Chemical Development, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877, USA
SOURCE: Journal of Organic Chemistry (2006), 71(23), 8864-8875
CODEN: JOCRAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel ruthenium carbene-catelyzed epimerization of vinylcyclopropanes is reported. The reaction rate strongly depends on the presence of ruthenium ligands in solution When the first-generation Grubbs catalyst is employed, a 5.3:1 equilibrium ratio of epimers is established quickly, but when a first-generation Hoveyda catalyst is employed, epimerization is observed only if an addnl. phosphine or nitrogen ligand is added. NMR and kinetic studies suggest that the isomerization reaction occurs through the intermediacy of a ruthenacyclopentene. The observation suggests that cyclopropylmethylidene ruthenium carbenes of synthetic utility may be accessible via ruthenacyclopentenes obtained via other routes.
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(7) OF 77 ...X + Z ===> AA...

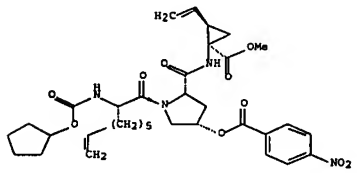


X



Z

(7) →



AA
YIELD 92%

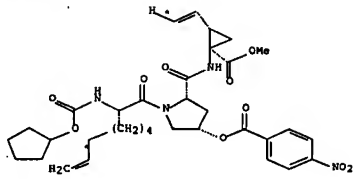
RX(7) RCT X 915317-30-5

STAGE(1)
RGT AB 7647-01-0 HCl
SOL 7732-18-5 Water, 123-91-1 Dioxane
CON 3 hours, room temperature

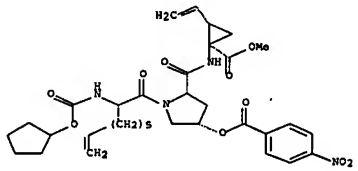
STAGE(2)
RCT Z 769167-55-7
RGT AC 125700-67-6 Benzotriazolium der, R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

PRO AA 912291-98-6

RX(10) OF 77 3 AI ===> AJ + AF + AA...



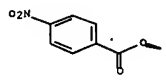
2 AI



AI

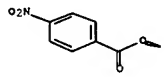
(10) →

PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-A



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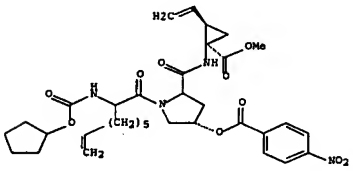
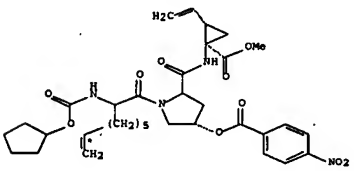


AA

RX(10) RCT AI 912291-94-2
PRO AJ 912291-95-3, AF 912291-99-7, AA 912291-98-6
CAT 172222-30-9 Ruthenium, dichloro(phenylmethylene)bis(tricyclohexylphosphine)-, (SP-5-31)-
SOL 108-88-3 PhMe
CON 60 deg C

RX(20) OF 77 2 AI + 2 G ===> BK + BL



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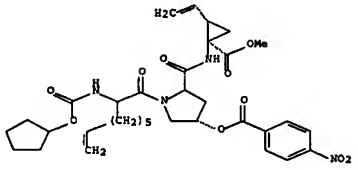
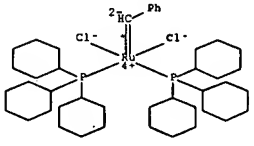


AI



2 G

(20) →

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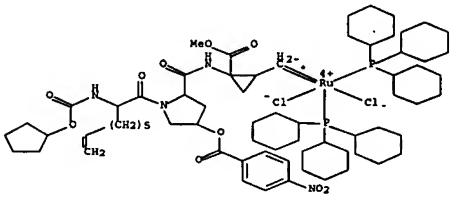
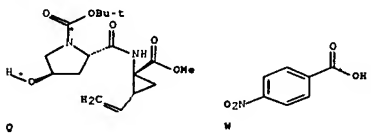


BL

RX(20) RCT AI 912291-94-2, G 172222-30-9
PRO BK 919530-94-2, BL 919530-95-3
SOL 1665-00-5 CD2Cl2

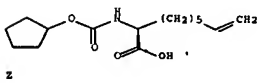
CON room temperature

RX(31) OF 77 COMPOSED OF RX(6), RX(7)
RX(31) Q + W + Z ===> AA



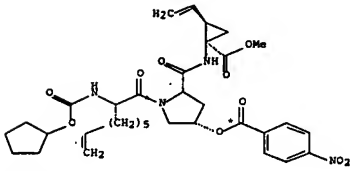
Q

W



Z

2 STEPS



AA
YIELD 92%

RX(6) RCT Q 915317-27-0, W 62-23-7

STAGE(1)
RGT H 603-35-0 PPh3
SOL 109-99-9 THF
CON room temperature -> 0 deg C

STAGE(2)
RGT Y 2446-83-5 N2(CO2CHMe2)2
SOL 109-99-9 THF
CON <5 deg C

PRO X 915317-30-5
NTE stereoselective

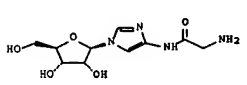
RX(7) RCT X 915317-30-5

STAGE(1)
RGT AB 7647-01-0 HCl
SOL 7732-18-5 Water, 123-91-1 Dioxane
CON 3 hours, room temperature

STAGE(2)
RCT Z 769167-55-7
RGT AC 125700-67-6 Benzotriazolium der, R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

PRO AA 912291-98-6

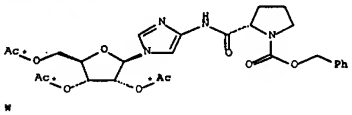
L5 ANSWER 2 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:62144 CASREACT Full-text
TITLE: Synthesis and biological evaluation of a new category of purine-nucleoside analogues
AUTHOR(S): Li, Da-Liang; Bao, Hong-Li; Tan, Qi-Tao; Ke, Yu-Ping; You, Tian-Pa
CORPORATE SOURCE: Department of Chemistry, University of Science and Technology of China, Hefei, Anhui, 230026, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (2005), 23(12), 1659-1664
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Shanghai Institute of Organic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

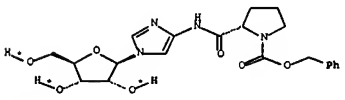
AB Convenient procedure for coupling of 1,2,3,5-tetra-O-acetyl-β-D- ribofuranose and 4-nitroimidazole was provided to obtain β-anomer as major product. A novel category of nucleoside analogs, e.g. I, with an imidazole base moiety bearing amino-acid residue was designed and synthesized to develop selective and effective antiviral agents. The title compds. were evaluated for the anti-HBV activity to find that only I exhibits cytotoxicity (MTT assay) at IC50 0.3436 μmol/L and anti-HBV activity at HbeAg and CC50 15.21 μmol/L.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(13) OF 51 ...W ===> AH



W

(13)



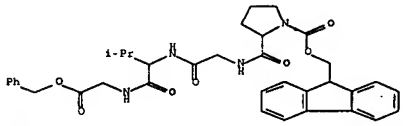
AH
YIELD 95%

RX(13) RCT W 851262-12-1
RGT AC 7664-41-7 NH3
PRO AH 917083-06-8
SOL 67-56-1 MeOH
CON 24 - 48 hours, room temperature

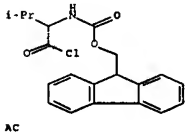
L5 ANSWER 3 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:419451 CASREACT Full-text
TITLE: Rapid and efficient synthesis of the pentapeptide of elastin protein and peptides containing highly hindered α,α-dialkyl amino acids employing Fmoc-amino acid chlorides under microwave irradiation in the solution phase
AUTHOR(S): Tantry, Subramanyam J.; Rao, R. V. Ramana; Babu, V. V. Suresh
CORPORATE SOURCE: Department of Studies in Chemistry, Bangalore University, Bangalore, 560 001, India
SOURCE: ARKIVOC (Gainesville, FL, United States) (2006), (1), 21-30
CODEN: AGFUAR
URL: http://www.arkat-usa.org/ark/journal/2006/I01_General/1576/05-1576B%20as%20published%20mainmanuscript.pdf
PUBLISHER: Arkat USA Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB A rapid and efficient synthesis of peptides in solution employing Fmoc-amino acid chlorides under microwave irradiation is described. A comparison study of the microwave assisted method with those of conventional peptide synthesis using acid chlorides and various coupling additives has been performed. It has been found that, in general, the formation of a peptide bond, employing Fmoc-amino acid chloride and zinc dust or TBDMS-OBt under microwave irradiation is complete in 30-45 s with 90% yield of pure isolated peptide. Employing zinc dust as a coupling additive, the synthesis of several dipeptides,

the pentapeptide fragment Fmoc-Val-Pro-Gly-Val-Gly- OBzl of elastin and the difficult highly hindered couplings of α,α-dialkylamino acids are reported.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(14) OF 31 ...AH + AC ===> AI

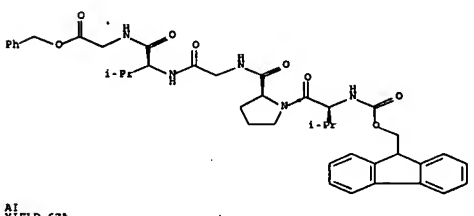


AH



AC

(14)



AI
YIELD 67%

RX(14) RCT AH 911858-48-5

STAGE(1)
RGT AG 4097-89-6 1,2-Ethanediamine, N1,N1-bis(2-aminoethyl)-
SOL 75-09-2 CH2Cl2
CON 20 minutes, room temperature

STAGE(2)
RCT AC 103321-53-5
RGT D 7440-66-6 Zn
SOL 75-09-2 CH2Cl2
CON 30 seconds

PRO AI 911058-49-6
NTE microwave irradiation in stage 2

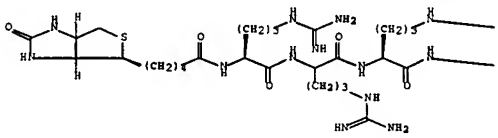
L5 ANSWER 4 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:351168 CASREACT Full-text
TITLE: Protease-Modulated Cellular Uptake of Quantum Dots
AUTHOR(S): Zhang, Yan; So, Min Kyung; Rao, Jianghong
CORPORATE SOURCE: Biophysics, Cancer Biology and Molecular Imaging Programs, Department of Radiology, Stanford University School of Medicine, Stanford, CA, 94305-5484, USA
SOURCE: Nano Letters (2006), 6(9), 1988-1992
CODEN: NALEFD; ISSN: 1530-6984
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quantum dots (QDs) are often cell-impermeable and require transporters to facilitate crossing over cell membranes. Here the authors present a simple and versatile method that utilizes enzymes, matrix metalloprotease 2 (MMP-2) and MMP-7, to modulate the cellular uptake of QDs. QD-peptide conjugates could be efficiently taken up into cells after the MMP treatment. This enzyme-modulated cellular uptake of QDs may be applied to other nanoparticles for biol. imaging and selective drug delivery into tumor cells.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 14 A + B ===> C

PAGE 1-A



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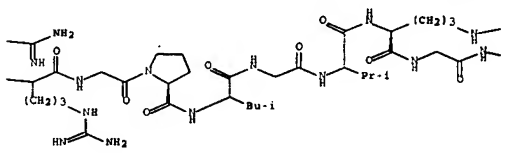

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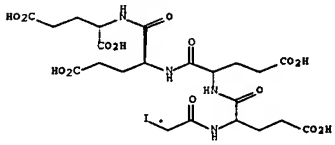
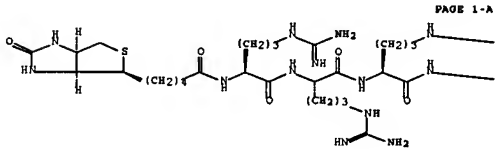
A



B

(1)

PAGE 1-A



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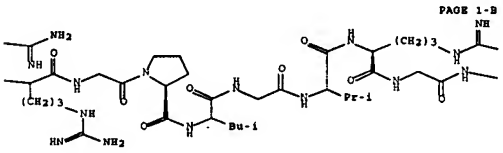

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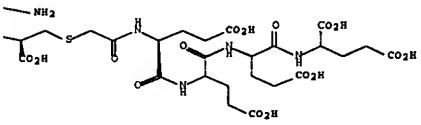
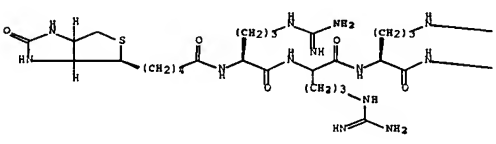


C

RX(1) RCT A 910217-61-7, B 910217-62-8
RGT D 7087-68-5 EtN(Pr-i)2
PRO C 910217-63-9

RX(4) OF 14 ...A + N ===> O

PAGE 1-A



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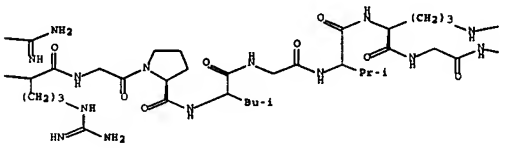

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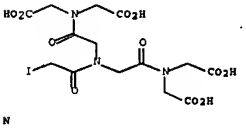
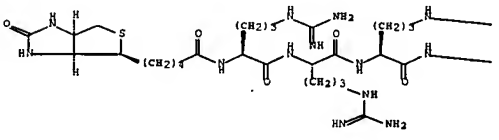
A



N

(4)

PAGE 1-A



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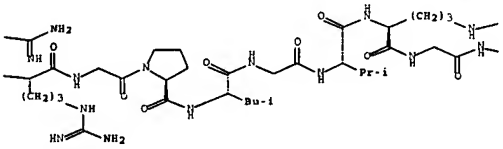

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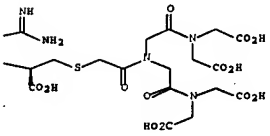
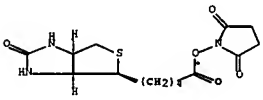


O

RX(4) RCT A 910217-61-7, N 910217-64-0
RGT D 7087-68-5 EtN(Pr-i)2
PRO O 910217-65-1
SOL 68-12-2 DMF

RX(6) OF 14 ...R + T ===> U



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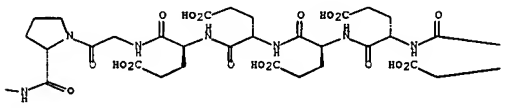
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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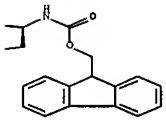

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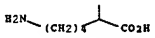
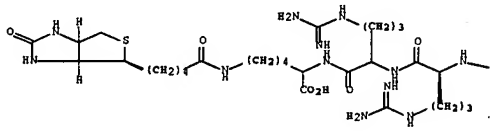


T

(6)

PAGE 1-A



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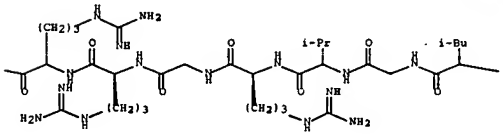

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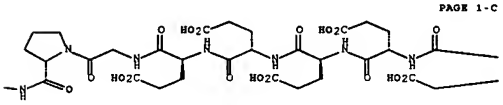

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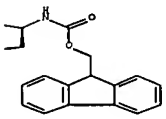
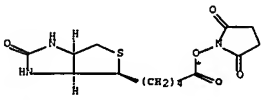


U

RX(6) RCT R 35013-72-0, T 910217-66-2
RGT S 538-75-0 DCC
PRO U 910217-67-3
SOL 68-12-2 DMF

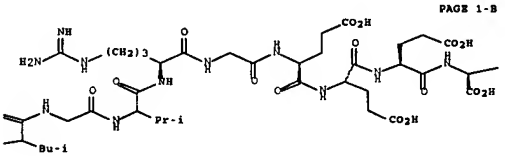
RX(7) OF 14 ...R + V ===> W



R

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



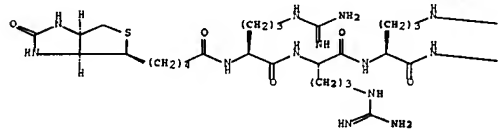
PAGE 1-C

PAGE 2-A

V

(7)

PAGE 1-A



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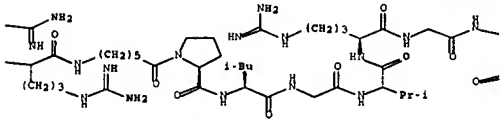

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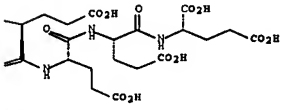
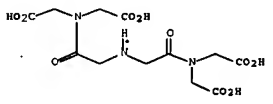


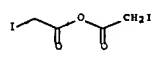
W

RX(7) RCT R 35013-72-0, V 910217-69-5
RGT S 538-75-0 DCC
PRO W 910217-70-8
SOL 68-12-2 DMF

RX(10) OF 14 COMPOSED OF RX(3), RX(4)
RX(10) G + M + A ===> O

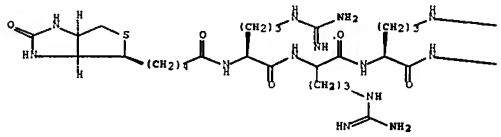


G



M

PAGE 1-A



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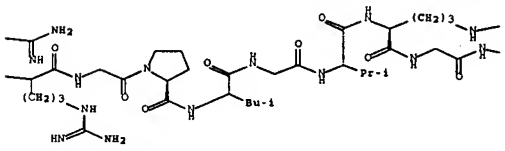
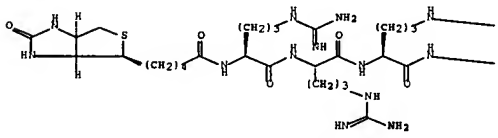


PAGE 1-C

A

2 STEPS

PAGE 1-A



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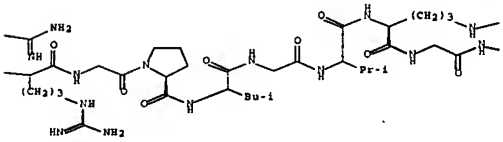

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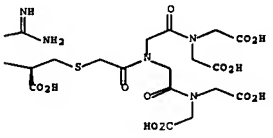
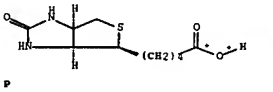


O

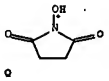
RX(3) RCT G 215391-21-2, M 54907-61-8
RGT D 7087-68-5 EtN(Pr-i)2
PRO N 910217-64-0
SOL 68-12-2 DMF

RX(4) RCT A 910217-61-7, N 910217-64-0
RGT D 7087-68-5 EtN(Pr-i)2
PRO O 910217-65-1
SOL 68-12-2 DMF

RX(11) OF 14 COMPOSED OF RX(5), RX(6)
RX(11) P + Q + T ===> U



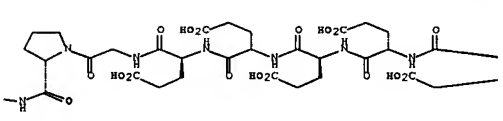
P



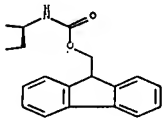
Q

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 1-C



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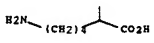
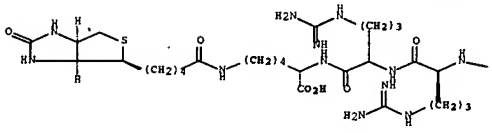


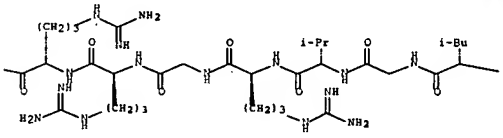
T

3 STEPS

PAGE 1-A



PAGE 1-B



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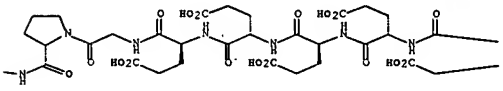

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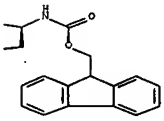
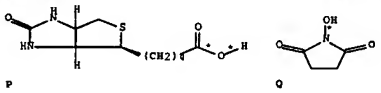


U

RX(5) RCT P 58-05-5, Q 6066-82-6
RGT S 538-75-0 DCC
PRO R 35013-72-0
SOL 68-12-2 DMF

RX(6) RCT R 35013-72-0, T 910217-66-2
RGT S 538-75-0 DCC
PRO U 910217-67-3
SOL 68-12-2 DMF

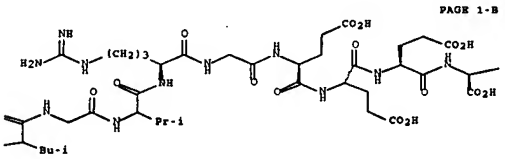
RX(12) OF 14 COMPOSED OF RX(5), RX(7)
RX(12) P + Q + V ===> W



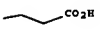
P Q

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 1-C

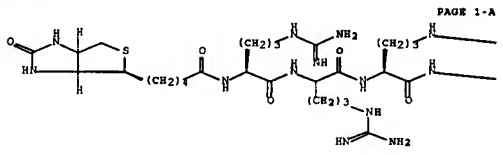


PAGE 2-A

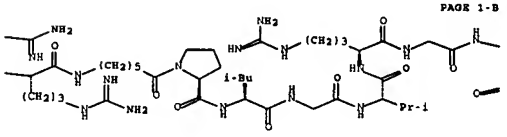
V

2 STEPS

PAGE 1-A



PAGE 1-B



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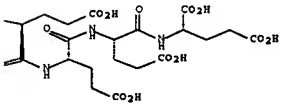
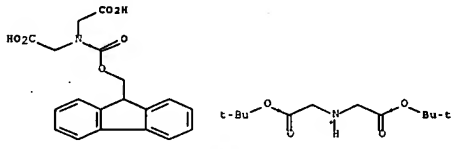


W

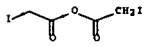
RX(5) RCT P 58-05-5, Q 6066-82-6
RGT S 538-75-0 DCC
PRO R 35013-72-0
SOL 68-12-2 DMF

RX(7) RCT R 35013-72-0, V 910217-69-5
RGT S 538-75-0 DCC
PRO W 910217-70-8
SOL 68-12-2 DMF

RX(14) OF 14 COMPOSED OF RX(2), RX(3), RX(4)
RX(14) 2 E + F + M + A ===> O

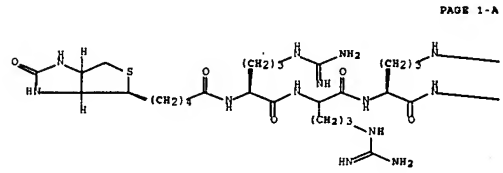


2 E F



H

PAGE 1-A



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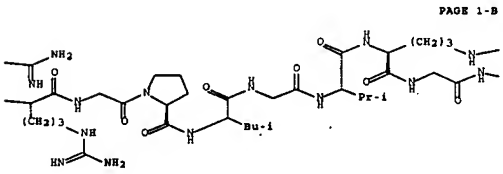

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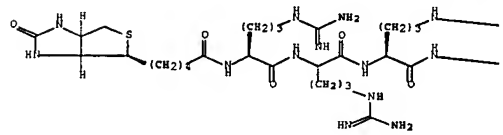
A

3 STEPS

PAGE 1-A



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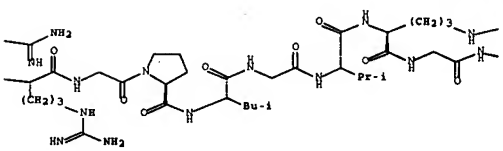
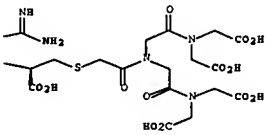


PAGE 1-C



O

RX(2) RCT E 112918-82-8, F 85916-13-8

STAGE(1)
RGT H 94790-37-1 HBTU, D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF

STAGE(2)
RGT I 110-89-4 Piperidine

STAGE(3)
RGT J 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO G 215391-21-2

RX(3) RCT G 215391-21-2, M 54907-61-8
RGT D 7087-68-5 EtN(Pr-i)2
PRO N 910217-64-0
SOL 68-12-2 DMF

RX(4) RCT A 910217-61-7, N 910217-64-0
RGT D 7087-68-5 EtN(Pr-i)2
PRO O 910217-65-1
SOL 68-12-2 DMF

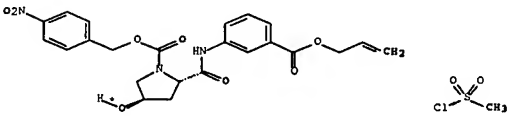
L5 ANSWER 5 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:124445 CASREACT Full-text
TITLE: Process for preparation of (2S,4S)-1-(4-nitrobenzyloxycarbonyl)-2-(3-(allyloxycarbonyl)phenylaminocarbonyl]pyrrolidine-4-thiol
INVENTOR(S): Zhang, Wanbin; Liu, Delong; Luo, Li; Xie, Fang
PATENT ASSIGNEE(S): Shanghai Jiao Tong University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1752073	A	20060329	CN 2005-10030662	20051020

PRIORITY APPLN. INFO.: CN 2005-10030662 20051020

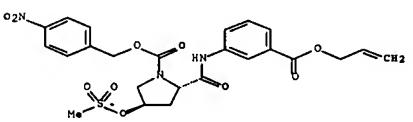
AB This invention relates to a method for preparation of (2S,4S)-1-(4-nitrobenzyloxycarbonyl)-2-(3-(allyloxycarbonyl)phenylaminocarbonyl]pyrroli dine-4-thiol, which comprises (1) reacting trans-4-hydroxy-L-proline and p-nitrobenzyloxycarbonyl chloride; (2) reacting m-nitrobenzoic acid and thionyl chloride, then reacting with allyl alc. for allyl m-nitrobenzoate; (3) tin dichloride reducing allyl m-nitrobenzoate for allyl m-aminobenzoate; (4) reacting product of step 1 and allyl m-aminobenzoate; (5) methanesulfonyl chloride treating product of step 4; (6) reacting product of step 5 with potassium thioacetate; (7) hydrolyzing product of step 6 for final product. This invention provides environment friendly method for preparation of title product with low cost.

RX(5) OF 34 ...Q + T ===> U...



Q T

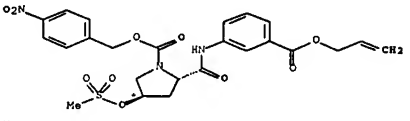
(5)



U

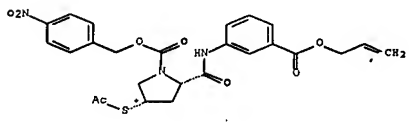
RX(5) RCT Q 896731-55-8, T 124-63-0
RGT L 121-44-8 Et3N
PRO U 896731-56-9
SOL 75-09-2 CH2Cl2
CON 40 minutes, room temperature

RX(6) OF 34 ...U + W ===> X...



U

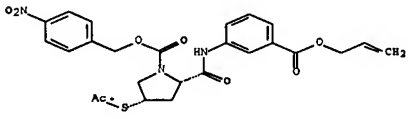
W



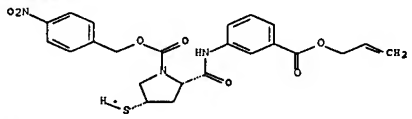
X

RX(6) RCT U 896731-56-9, W 10387-40-3
PRO X 153774-58-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, room temperature
SUBSTAGE(2) room temperature -> 70 deg C
SUBSTAGE(3) 5 hours, 70 deg C

RX(7) OF 34 ...X ===> Z



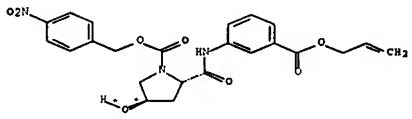
X



Z

RX(7) RCT X 153774-58-4
RGT AA 1310-73-2 NaOH
PRO Z 153775-54-3
SOL 107-18-6 Allyl alcohol
CON 20 minutes, 0 deg C
NTE 40% overall yield from 5

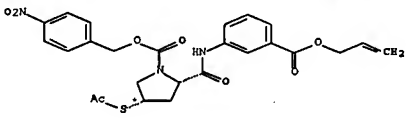
RX(12) OF 34 COMPOSED OF RX(5), RX(6)
RX(12) Q + T + W ===> X



Q

T

W

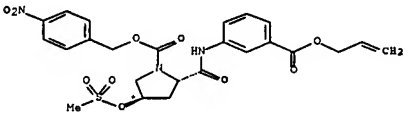


X

RX(5) RCT Q 896731-55-8, T 124-63-0
RGT L 121-44-8 Et3N
PRO U 896731-56-9
SOL 75-09-2 CH2Cl2
CON 40 minutes, room temperature

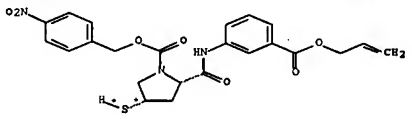
RX(6) RCT U 896731-56-9, W 10387-40-3
PRO X 153774-58-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, room temperature
SUBSTAGE(2) room temperature -> 70 deg C
SUBSTAGE(3) 5 hours, 70 deg C

RX(13) OF 34 COMPOSED OF RX(6), RX(7)
RX(13) U + W ===> Z



U

W

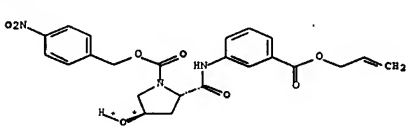


Z

RX(6) RCT U 896731-56-9, W 10387-40-3
PRO X 153774-58-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, room temperature
SUBSTAGE(2) room temperature -> 70 deg C
SUBSTAGE(3) 5 hours, 70 deg C

RX(7) RCT X 153774-58-4
RGT AA 1310-73-2 NaOH
PRO Z 153775-54-3
SOL 107-18-6 Allyl alcohol
CON 20 minutes, 0 deg C
NTE 40% overall yield from 5

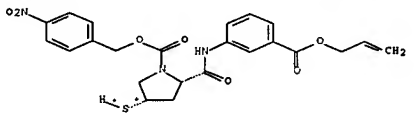
RX(23) OF 34 COMPOSED OF RX(5), RX(6), RX(7)
RX(23) Q + T + W ===> Z



Q

T

W



Z

RX(5) RCT Q 896731-55-8, T 124-63-0
RGT L 121-44-8 Et3N
PRO U 896731-56-9
SOL 75-09-2 CH2Cl2
CON 40 minutes, room temperature

RX(6) RCT U 896731-56-9, W 10387-40-3
PRO X 153774-58-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, room temperature
SUBSTAGE(2) room temperature -> 70 deg C
SUBSTAGE(3) 5 hours, 70 deg C

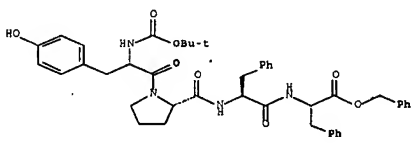
RX(7) RCT X 153774-58-4
RGT AA 1310-73-2 NaOH
PRO Z 153775-54-3
SOL 107-18-6 Allyl alcohol
CON 20 minutes, 0 deg C
NTE 40% overall yield from 5

L5 ANSWER 6 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:117514 CASREACT Full-text
TITLE: 6-N,N-Dimethylamino-2,3-naphthalimide: A New Environment-Sensitive Fluorescent Probe in δ- and μ-Selective Opioid Peptides
AUTHOR(S): Vazquez, M. Eugenio; Blanco, Juan B.; Salvadori, Severo; Trapella, Claudio; Argazzi, Roberto; Bryant, Sharon D.; Jinsmaa, Yunden; Lazarus, Lawrence H.; Negri, Lucia; Giannini, Elisa; Lattanzi, Roberta; Colucci, Mariantonella; Balboni, Gianfranco
CORPORATE SOURCE: Departamento de Química Organica y Unidad Asociada al CSIC, Universidad de Santiago de Compostela, Santiago de Compostela, 15782, Spain
SOURCE: Journal of Medicinal Chemistry (2006), 49(12), 3653-3658
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new environment-sensitive fluorophore, 6-N,N-(dimethylamino)-2,3- naphthalimide (6DMN) was introduced in the δ-selective opioid peptide agonist H-Dmt-Tic-Glu-NH2 and in the μ-selective opioid peptide agonist endomorphin-2 (H-Tyr-Pro-Phe-Phe-NH2). Environment-sensitive fluorophores are a special class of chromophores that generally exhibit a low quantum yield in aqueous solution but become highly fluorescent in nonpolar solvents or when bound to hydrophobic sites in proteins or membranes. New fluorescent δ-selective irreversible antagonists (H-Dmt-Tic-Glu-NH-(CH2)5-CO-Dap(6DMN)-NH2 and H-Dmt-Tic-Glu-Dap(6DMN)-NH2) were identified as potential fluorescent probes showing good properties

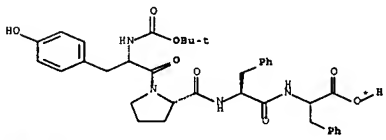
for use in studies of distribution and internalization of δ receptors by confocal laser scanning microscopy.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(6) OF 25 ...Y ===> AB...



Y

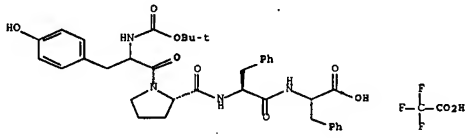
(6)



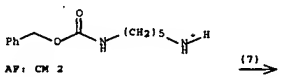
AB
YIELD 96%

RX(6) RCT Y 897959-54-5
RGT AC 1333-74-0 H2
PRO AB 897959-57-8
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(7) OF 25 ...AB + AF ===> AG...



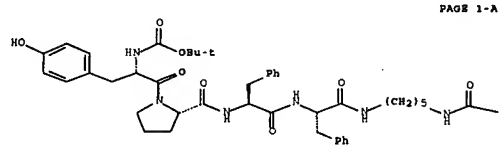
AB AF: CM 1



AF: CM 2

(7)

PAGE 1-A



PAGE 1-B

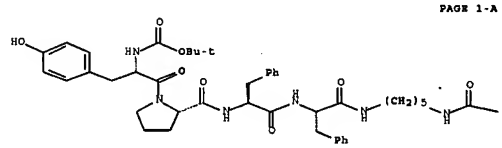
AG
YIELD 83%

RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA

25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

RX(8) OF 25 ...AG ===> AH...

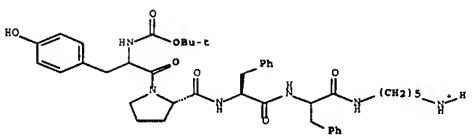
PAGE 1-A



PAGE 1-B

AG

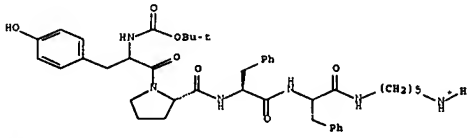
(8)



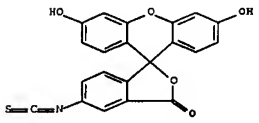
AH
YIELD 83%

RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(9) OF 25 ...AH + AI ===> AJ...



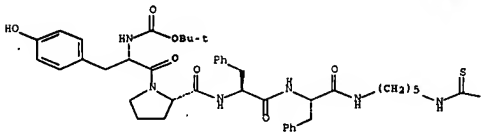
AH



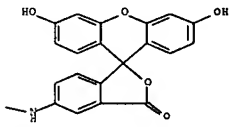
AI

(9)

PAGE 1-A



PAGE 1-B

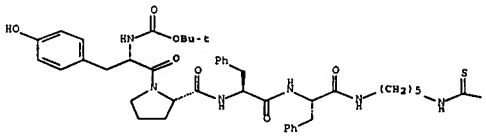


AJ
YIELD 50%

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

RX(10) OF 25 ...AJ ===> AN

PAGE 1-A



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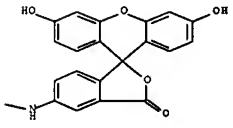
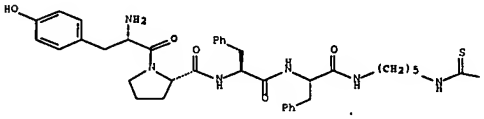


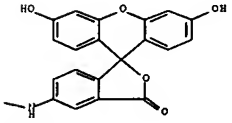
AJ

(10)

PAGE 1-A



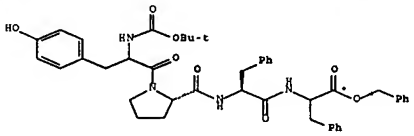
PAGE 1-B



AN
YIELD 90%

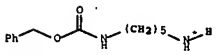
RX(10) RCT AJ 897959-62-5
RGT M 76-05-1 F3CCO2H
PRO AN 897959-46-5
SOL 7732-18-5 Water
CON 30 minutes, room temperature

RX(12) OF 25 COMPOSED OF RX(6), RX(7)
RX(12) Y + AF ===> AG



Y

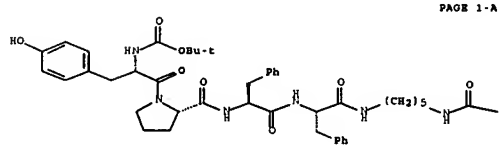
AF: CM 1



AF: CM 2

2 STEPS

PAGE 1-A



PAGE 1-B

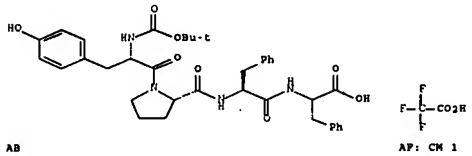
AG
YIELD 83%

RX(6) RCT Y 897959-54-5
RGT AC 1333-74-0 H2
PRO AB 897959-57-8

CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

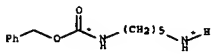
RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA
25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

RX(13) OF 25 COMPOSED OF RX(7), RX(8)
RX(13) AB + AF ===> AH



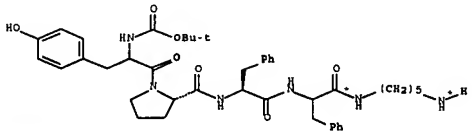
AB

AF: CM 1



AF: CM 2

2 STEPS



AH
YIELD 83%

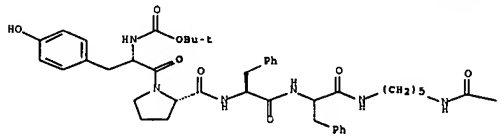
RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA

25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

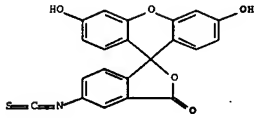
RX(14) OF 25 COMPOSED OF RX(8), RX(9)
RX(14) AG + AI ===> AJ

PAGE 1-A



PAGE 1-B

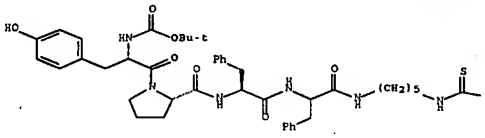
AG



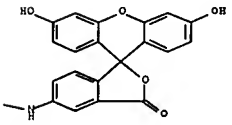
AI

2 STEPS

PAGE 1-A



PAGE 1-B

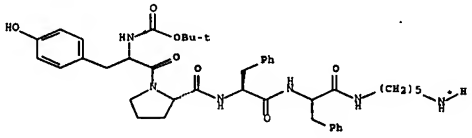


AJ
YIELD 50%

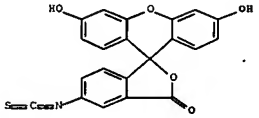
RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

RX(15) OF 25 COMPOSED OF RX(9), RX(10)
RX(15) AH + AI ===> AN



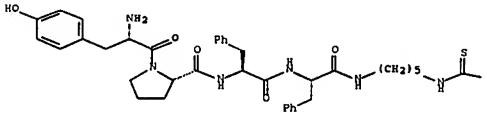
AH



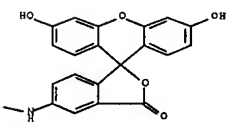
AI

2 STEPS

PAGE 1-A



PAGE 1-B

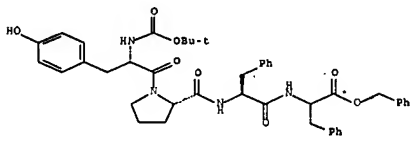


AN
YIELD 90%

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

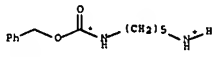
RX(10) RCT AJ 897959-62-5
RGT M 76-05-1 F3CCO2H
PRO AN 897959-46-5
SOL 7732-18-5 Water
CON 30 minutes, room temperature

RX(17) OF 25 COMPOSED OF RX(6), RX(7), RX(8)
RX(17) Y + AF ===> AH



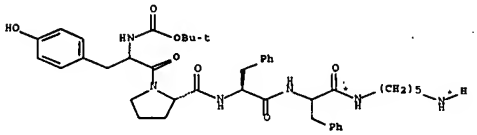
Y

AF: CM 1



AF: CM 2

3 STEPS



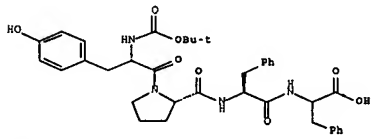
AH
YIELD 83%

RX(6) RCT Y 897959-54-5
RGT AC 1333-74-0 H2
PRO AB 897959-57-8
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA 25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

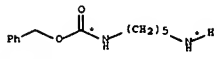
RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(19) OF 25 COMPOSED OF RX(7), RX(8), RX(9)
RX(19) AB + AF + AI ===> AJ

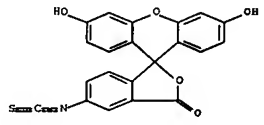


AB

AF: CM 1



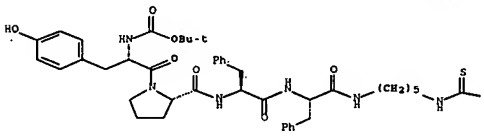
AF: CM 2



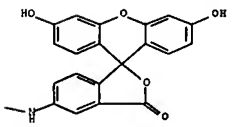
AI

3 STEPS

PAGE 1-A



PAGE 1-B



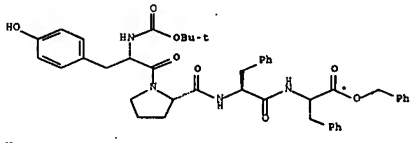
AJ
YIELD 50%

RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA 25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

RX(20) OF 25 COMPOSED OF RX(6), RX(7), RX(8), RX(9)
RX(20) Y + AF + AI ===> AJ



Y

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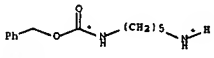
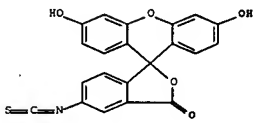


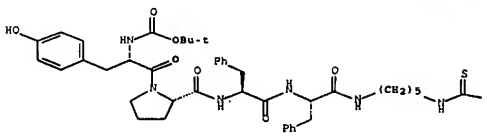
AF: CM 2



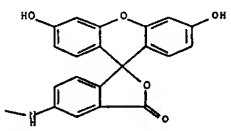
AI

4 STEPS

PAGE 1-A



PAGE 1-B



AJ
YIELD 50%

RX(6) RCT Y 897959-54-5
RGT AC 1333-74-0 H2
PRO AB 897959-57-8
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

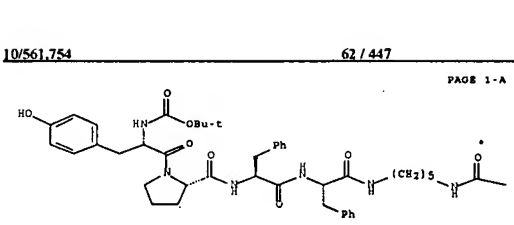
RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA 25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

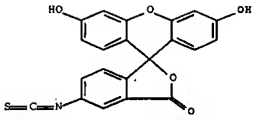
RX(21) OF 25 COMPOSED OF RX(8), RX(9), RX(10)
RX(21) AG + AI ===> AN

PAGE 1-A



PAGE 1-B

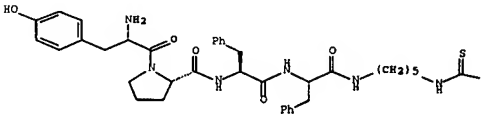
AG



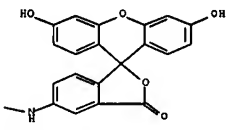
AI

3 STEPS

PAGE 1-A



PAGE 1-B



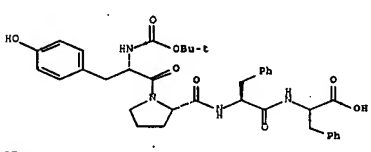
AN
YIELD 90%

RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour; room temperature

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

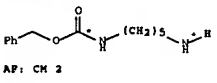
RX(10) RCT AJ 897959-62-5
RGT M 76-05-1 F3CCO2H
PRO AN 897959-46-5
SOL 7732-18-5 Water
CON 30 minutes, room temperature

RX(22) OF 25 COMPOSED OF RX(7), RX(8), RX(9), RX(10)
RX(22) AB + AF + AI ===> AN

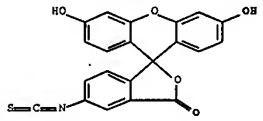


AB

AF: CM 1



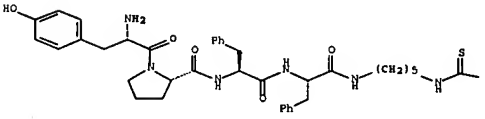
AF: CM 2



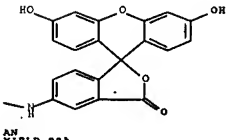
AI

4 STEPS

PAGE 1-A



PAGE 1-B



AN
YIELD 90%

RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA 25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C

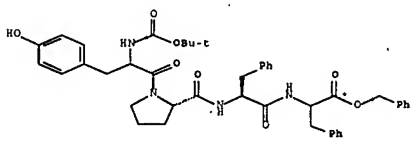
SUBSTAGE(2) 24 hours, room temperature

RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

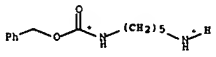
RX(10) RCT AJ 897959-62-5
RGT M 76-05-1 F3CCO2H
PRO AN 897959-46-5
SOL 7732-18-5 Water
CON 30 minutes, room temperature

RX(24) OF 25 COMPOSED OF RX(6), RX(7), RX(8), RX(9), RX(10)
RX(24) Y + AF + AI ===> AN

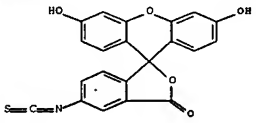


Y

AF: CM 1



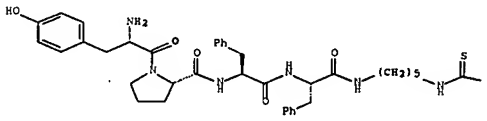
AF: CM 2



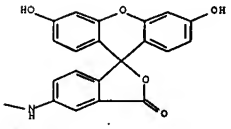
AI

5 STEPS

PAGE 1-A



PAGE 1-B



AN
YIELD 90%

RX(6) RCT Y 897959-54-5
RGT AC 1333-74-0 H2
PRO AB 897959-57-8
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(7) RCT AB 897959-57-8, AF 897959-68-1
RGT K 2592-95-2 1-Benzotriazolol, Z 109-02-4 N-Methylmorpholine, AA 25952-53-8 EDAP
PRO AG 897959-59-0
SOL 68-12-2 DMF
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 24 hours, room temperature

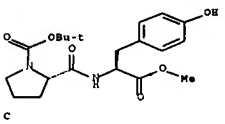
RX(8) RCT AG 897959-59-0
RGT AC 1333-74-0 H2
PRO AH 897959-61-4
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON 1 hour, room temperature

RX(9) RCT AH 897959-61-4, AI 3326-32-7
RGT AK 121-44-8 Et3N
PRO AJ 897959-62-5
SOL 64-17-5 EtOH, 109-99-9 THF
CON 24 hours, room temperature
NTE in the dark

RX(10) RCT AJ 897959-62-5
RGT M 76-05-1 F3CCO2H
PRO AN 897959-46-5
SOL 7732-18-5 Water
CON 30 minutes, room temperature

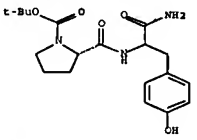
L5 ANSWER 7 OF 50 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:350944 CASREACT Full-text
TITLE: Application of triazine "superactive esters" in the repetitive synthesis of oligopeptides. Part 1. Synthesis of [54-59] fragment of human β-casein
AUTHOR(S): Kaminski, Zbigniew J.; Saleh, Bashar; Kolesinska, Beata; Redlinski, Adam; Rudzinski, Juliusz
CORPORATE SOURCE: Institute of Organic Chemistry, Technical University of Lodz, Lodz, 90-924, Pol.
SOURCE: Acta Poloniae Pharmaceutica (2005), 62(1), 53-57
CODEN: APPHAX; ISSN: 0001-6837
PUBLISHER: Polish Pharmaceutical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new synthetic protocol which considerably improves the classic REMA (repetitive excess mixed anhydrides) procedure is proposed. The modification is based on the application of triazine "superactive esters" as superior substitutes for mixed anhydrides, which have been used as acylating reagent in the classical procedure. The improved repetitive procedure in solution was applied to the preparation of [54-59] fragment of human β-casein. The structure and high purity of the intermediates, as well as of the final products, was confirmed by FAB-MS, 1H-NMR and HPLC.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 9 ...C ===> G...



C

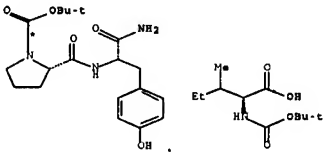
(2)



G
YIELD 80%

RX(2) RCT C 19669-38-6
RGT H 7664-41-7 NH3
PRO G 200954-43-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) <0 deg C
SUBSTAGE(2) <0 deg C -> room temperature
SUBSTAGE(3) 72 hours, room temperature

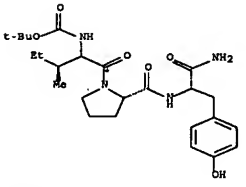
RX(3) OF 9 ...G + J ===> K



G

J

(3)



K
YIELD 95%

RX(3) RCT G 200954-43-4

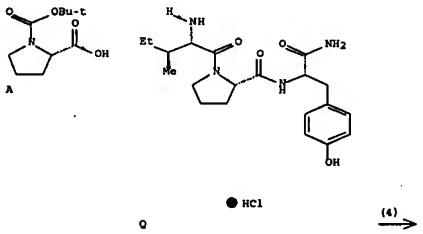
STAGE(1)
RGT L 7647-01-0 HCl
SOL 64-19-7 AcOH
CON room temperature

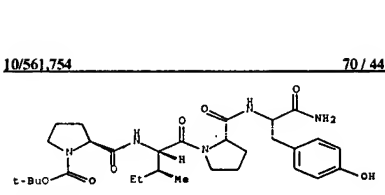
STAGE(2)
RCT J 13139-16-7
RGT D 3140-73-6 Cl-(MeO)2-s-triazine, E 109-02-4 N-Methylmorpholine
SOL 109-99-9 THF, 68-12-2 DMF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 4 hours, 0 deg C
SUBSTAGE(4) 3 hours, 0 deg C
SUBSTAGE(5) 0 deg C -> room temperature
SUBSTAGE(6) overnight, room temperature

STAGE(3)
RGT M 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, room temperature

PRO K 881492-63-3

RX(4) OF 9 A + Q ===> R





R
YIELD 82%

RX(4) RCT A 15761-39-4

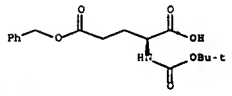
STAGE(1)
RGT D 3140-73-6 Cl-(MeO)2-s-triazine, E 109-02-4 N-Methylmorpholine
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 4 hours, 0 deg C

STAGE(2)
RCT Q 872333-21-6
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) overnight, room temperature

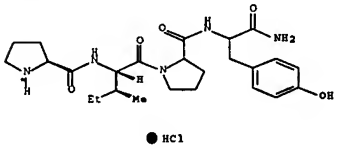
STAGE(3)
RGT M 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, room temperature

PRO R 881492-64-4

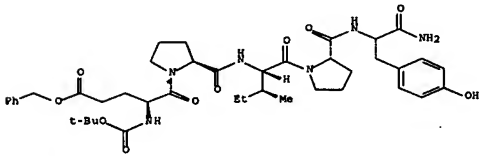
RX(5) OF 9 S + T ===> U



S



T
(5)



U
YIELD 98%

RX(5) RCT S 13574-13-5

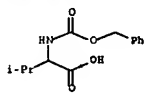
STAGE(1)
RGT D 3140-73-6 Cl-(MeO)2-s-triazine, E 109-02-4 N-Methylmorpholine
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 4 hours, 0 deg C

STAGE(2)
RCT T 881492-67-7
CON SUBSTAGE(1) 3 hours, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) overnight, room temperature

STAGE(3)
RGT M 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, room temperature

PRO U 881492-65-5

RX(6) OF 9 V + W ===> X

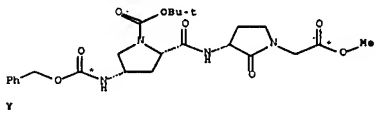


V

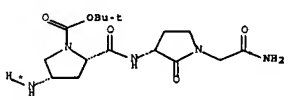
<------User Break------>

RX(33) RCT AO 99298-06-3, BO 874163-26-5
PRO BR 874163-22-1
SOL 75-05-8 MeCN
CON 18 hours, reflux

RX(47) OF 285 COMPOSED OF RX(11), RX(15)
RX(47) Y ===> AS



Y
2 STEPS



AS
YIELD 92%

=>
=> d hist

(FILE 'HOME' ENTERED AT 08:18:24 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 08:18:37 ON 30 MAY 2007
L1 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:19:13 ON 30 MAY 2007

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L2              0 S L1 SSS SAM
L3              1 S L1 SSS FULL

     FILE 'REGISTRY' ENTERED AT 08:21:37 ON 30 MAY 2007
L4              STRUCTURE UPLOADED

     FILE 'CASREACT' ENTERED AT 08:21:56 ON 30 MAY 2007
L5            50 S L4

=> s l5 not py>2003
COMMAND INTERRUPTED
REENTER FILE 'CASREACT'
AND TRY AGAIN, OR ENTER '?' FOR MORE INFORMATION.
Your command did not complete due to a temporary system problem.  To
recover, reenter the file you are in now.  Then, any command that is
normally available to you may be used.  No cost summary for the
current file will be displayed.  After reentering the current file you
may retry your command.  Also, you may wish to SAVE your search
query.  This can be done in any file.  If you cannot access your
current file, or if your command fails a second time, notify the Help
Desk.  Enter "HELP STN" for information on contacting the nearest STN
Help Desk by telephone or by using the SEND command in STNMAIL file.

=> file casreact
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                               1.80      124.54

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY     SESSION
CA SUBSCRIBER PRICE                               0.00       -0.73

FILE 'CASREACT' ENTERED AT 08:24:06 ON 30 MAY 2007
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FILE CONTENT:1840 - 27 May 2007 VOL 146 ISS 23

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**********************************************************
*                                                        *
*     CASREACT now has more than 12 million reactions    *
*                                                        *
**********************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> s l5 not py>2003
        101431 PY>2003
L6           28 L5 NOT PY>2003

=> d ibib abs hit 1-10
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L6   ANSWER 1 OF 28  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        140:287687  CASREACT  Full-text
TITLE:                   Synthetic glycopeptides of the tandem repeat sequence
                         of the epithelial mucin MUC4 with tumor-associated
                         carbohydrate antigens
AUTHOR(S):               Brocke, Constanze; Kunz, Horst
CORPORATE SOURCE:        Institut fuer Organische Chemie, Johannes
                         Gutenberg-Universitaet Mainz, Mainz, 55128, Germany
SOURCE:                  Synlett (2003), (13), 2052-2056
                         CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER:               Georg Thieme Verlag
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Glycohexadecapeptides representing the tandem repeat sequence of the epithelial mucin MUC4
     were prepared by applying a solid-phase methodol. The required glycosyl amino acid
     building blocks containing the tumor-associated saccharide antigens TN-, T,- sialyl-TN,
     (2,6)- and (2,3)-sialyl-T were synthesized according to a straightforward biomimetic
     strategy by step-wise extension of the saccharide side chain of a Fmoc-protected
     galactosamine threonine tert-Bu ester.
REFERENCE COUNT:         43    THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(20) OF 187    ...BK ===> BL

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

                                                                PAGE 1-B
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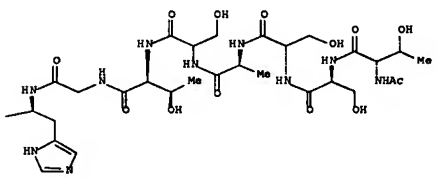

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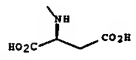

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BK

(20)
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

                                                                PAGE 1-B
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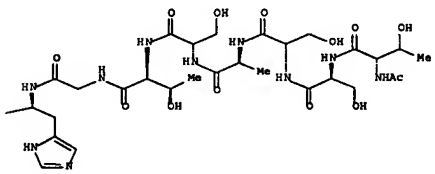

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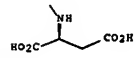

```
BL
YIELD 80%

RX(20)    RCT  BK 673476-54-5

            STAGE(1)
              RGT  BI 1333-74-0 H2
              CAT  7440-05-3 Pd
              SOL  67-56-1 MeOH
              CON  room temperature

            STAGE(2)
              RGT  C 124-41-4 NaOMe
              SOL  67-56-1 MeOH
              CON  room temperature, pH 9

          PRO  BL 673476-46-5

RX(21) OF 187    ...BM ===> BN

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
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                                                                PAGE 1-B
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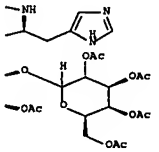

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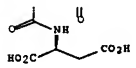

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BM

(21)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
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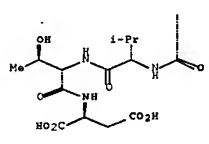

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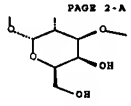

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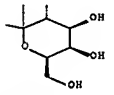


BN
YIELD 72%

RX(21) RCT BM 688348-62-1

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

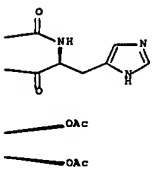
STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 9

PRO BN 673476-47-6

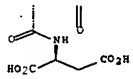
RX(22) OF 187 ...BO ===> BP

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 2-A



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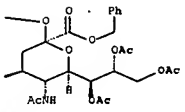
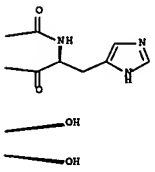


BO

(22)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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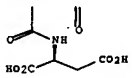

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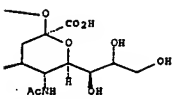


BP
YIELD 55%

RX(22) RCT BO 673476-56-7

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 9

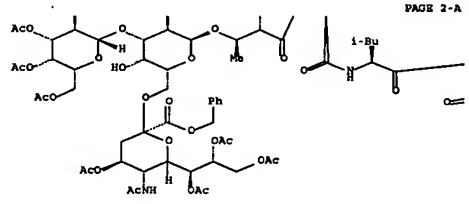
PRO BP 673476-48-7

RX(23) OF 187 ...BQ ===> BR

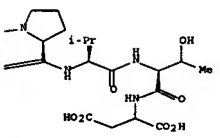
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B

PAGE 2-A



PAGE 2-B



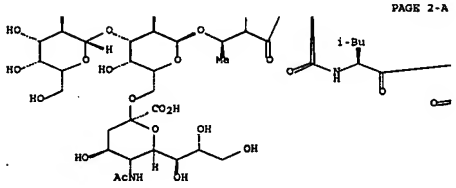
BQ

(23)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B

PAGE 2-A



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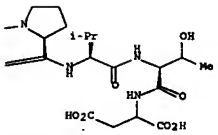


BR
YIELD 64 %

RX(23) RCT BQ 673476-63-2

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 9

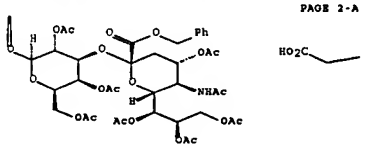
PRO BR 673476-49-8

RX(24) OF 187 ...BS ===> BT

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



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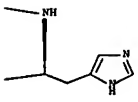
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

(24)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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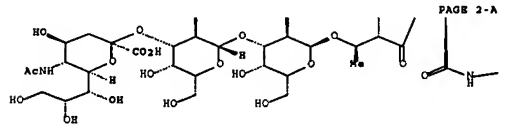

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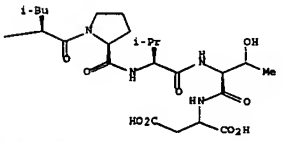


BT
YIELD 59 %

RX(24) RCT BS 673476-58-9

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 10

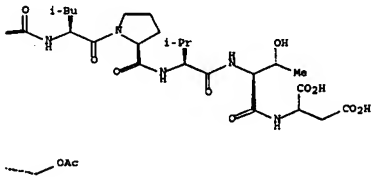
STAGE(3)
RGT BU 1310-73-2 NaOH
SOL 7732-18-5 Water
CON room temperature, pH 11.5

PRO BT 673476-50-1

RX(25) OF 187 ...BV ===> BW

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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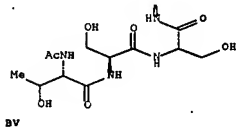
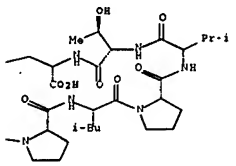


BV

(25)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-B

BW
YIELD 75%

RX(25) RCT BV 673476-59-0

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 9

PRO BW 673476-51-2

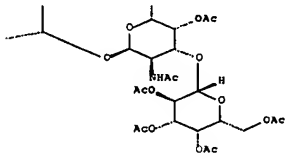
RX(26) OF 187 ...BX ===> BY

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-B



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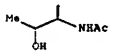

BX

(26)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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BY
YIELD 67%

RX(26) RCT BX 666348-64-3

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 9

PRO BY 673476-52-3

RX(27) OF 187 ...BZ ===> CA

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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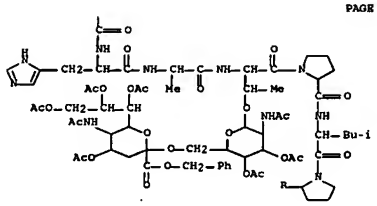
PAGE 2-A



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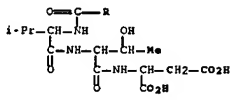


BZ

(27)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(27) RCT BZ 673476-61-4

STAGE(1)
RGT BI 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT C 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON room temperature, pH 9

PRO CA 673476-53-4

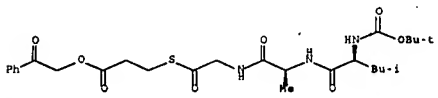
L6 ANSWER 2 OF 28 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:236064 CASREACT Full-text
TITLE: Application of Pac ester in thioester method for the synthesis of cyclopentapeptides
AUTHOR(S): Liu, Mian; Tian, Gui-Ling; Ye, Yun-Hua
CORPORATE SOURCE: Key Laboratory of Bioorganic Chemistry and Molecular Engineering, Ministry of Education, Department of Chemistry, Peking University, Beijing, 100871, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (2003), 21(7), 864-870
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The thioester method for the synthesis of cyclopeptides is improved by using Pac (Pac = phenacyl, CH2COC6H5) ester as a protecting group for 3-mercaptopropionic acid. The Pac group is easily removed from the C-terminal using zinc in acetic acid. The protected peptide thioesters synthesized by the improved method are easily purified for use in subsequent cyclization. Furthermore, this method is flexible for use in peptide chain

elongation, either from the C-terminal or the N-terminal. Two N-protected pentapeptide thioesters, Boc-Pro-Tyr-Leu-Ala-Gly- SCH2CH2COOPac and Boc-Ala-Tyr-Leu-Ala-Gly-SCH2CH2COOPac, were synthesized by the improved thioester method. After deprotecting the Pac ester with zinc in aqueous acetic acid and the Boc group with trifluoroacetic acid in CH2Cl2, two free pentapeptide thioesters were obtained. Ag+-assisted cyclization in acetate buffered solution afforded cyclic pentapeptides cyclo(Pro-Tyr-Leu-Ala-Gly) and cyclo(Ala-Tyr-Leu-Ala-Gly). Effects of different buffer pH, Ag+ concns., etc. on the cyclization were studied.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(4) OF 77 ...N + O ===> P...



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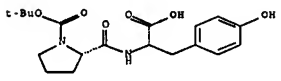
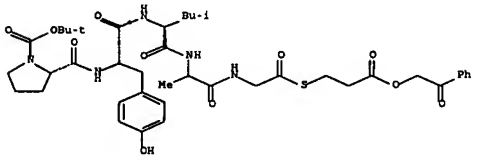


O

(4) ⟶



P
YIELD 51%

RX(4) RCT N 503440-97-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt

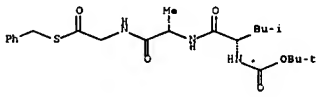
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

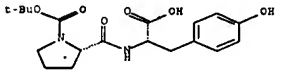
STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO P 503440-98-0
NTE intermediate product could be isolated

RX(15) OF 77 ...AK + O ===> AL...

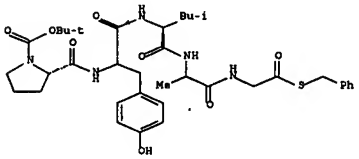


AK



O

(15) ⟶



AL
YIELD 70%

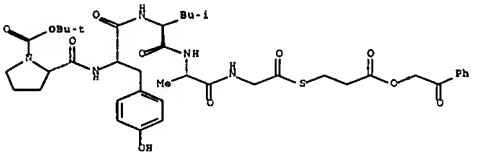
RX(15) RCT AK 667905-07-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON overnight, room temperature

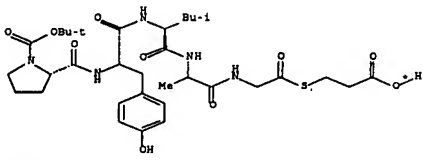
PRO AL 667905-09-1
NTE intermediate product could be isolated

RX(16) OF 77 ...P ===> T...



P

(16) ⟶

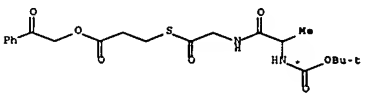


T
YIELD 83%

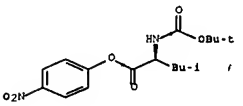
RX(16) RCT P 503440-98-0
RGT AP 64-19-7 AcOH, AQ 7440-66-6 Zn
PRO T 854749-15-8
SOL 64-19-7 AcOH, 7732-18-5 Water

CON 1 hour, room temperature

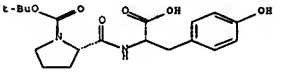
RX(20) OF 77 COMPOSED OF RX(3), RX(4)
RX(20) O + M + O ===> P



G

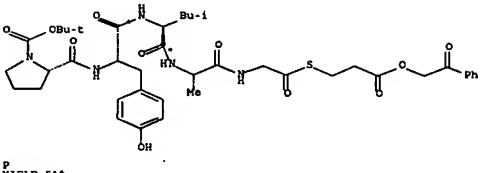


M



O

2 STEPS ⟶



P
YIELD 51%

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

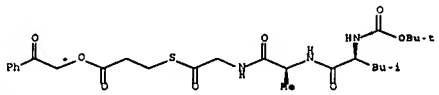
STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

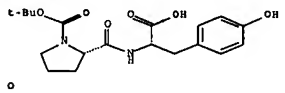
STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO P 503440-98-0
NTE intermediate product could be isolated

RX(22) OF 77 COMPOSED OF RX(4), RX(16)
RX(22) N + O ===> T

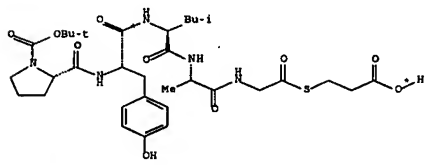


N



O

2 STEPS



T
YIELD 83%

RX(4) RCT N 503440-97-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

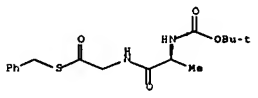
STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

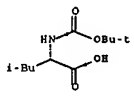
PRO P 503440-98-0
NTE intermediate product could be isolated

RX(16) RCT P 503440-98-0
RGT AP 64-19-7 AcOH, AQ 7440-66-6 Zn
PRO T 854749-15-8
SOL 64-19-7 AcOH, 7732-18-5 Water
CON 1 hour, room temperature

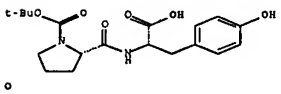
RX(28) OF 77 COMPOSED OF RX(12), RX(15)
RX(28) AH + AJ + O ===> AL



AH

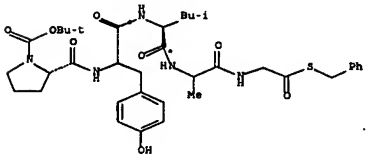


AJ



O

2 STEPS



AL
YIELD 70%

RX(12) RCT AH 667905-06-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT AJ 13139-15-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON 24 hours, room temperature

PRO AK 667905-07-9
NTE intermediate product could be isolated

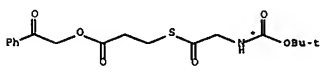
RX(15) RCT AK 667905-07-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

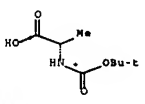
STAGE(2)
RCT O 132149-57-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON overnight, room temperature

PRO AL 667905-09-1
NTE intermediate product could be isolated

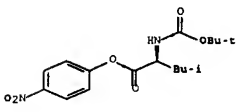
RX(35) OF 77 COMPOSED OF RX(2), RX(3), RX(4)
RX(35) C + F + M + O ===> P



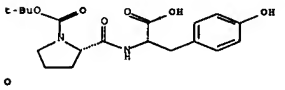
C



F

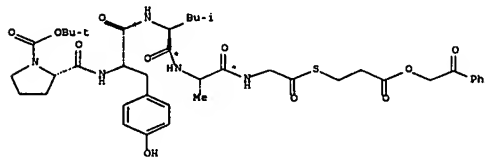


M



O

3 STEPS



P
YIELD 51%

RX(2) RCT C 503440-95-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO G 503440-96-8
NTE intermediate product could be isolated

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

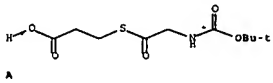
STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

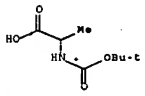
PRO P 503440-98-0
NTE intermediate product could be isolated

RX(37) OF 77 COMPOSED OF RX(1), RX(2), RX(3), RX(4)
RX(37) A + B + F + M + O ===> P

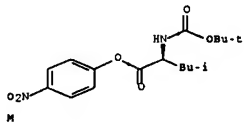


A

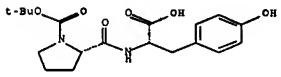
B



F

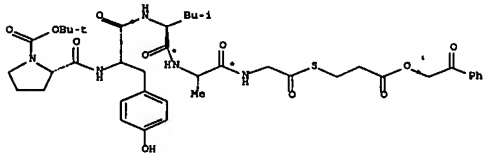


M



O

4
STEPS



P
YIELD 51%

RX(1) RCT A 133367-03-0, B 70-11-1
RGT D 7087-68-5 EtN(Pr-i)2
PRO C 503440-95-7
SOL 68-12-2 DMF
CON overnight, room temperature

RX(2) RCT C 503440-95-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO G 503440-96-8
NTE intermediate product could be isolated

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

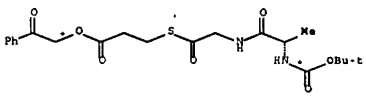
STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

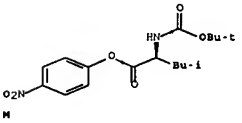
STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO P 503440-98-0
NTE intermediate product could be isolated

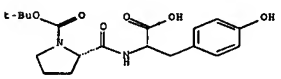
RX(39) OF 77 COMPOSED OF RX(3), RX(4), RX(16)
RX(39) G + M + O ===> T



G

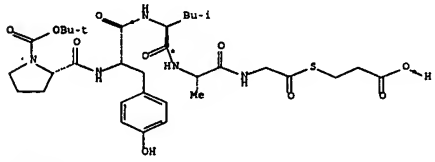


M



O

3
STEPS



T
YIELD 83%

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

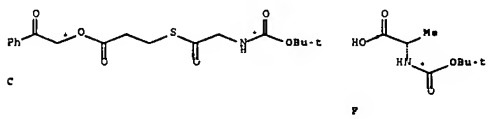
STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO P 503440-98-0
NTE intermediate product could be isolated

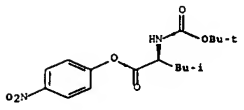
RX(16) RCT P 503440-98-0
RGT AP 64-19-7 AcOH, AQ 7440-66-6 Zn
PRO T 854749-15-8
SOL 64-19-7 AcOH, 7732-18-5 Water

CON 1 hour, room temperature

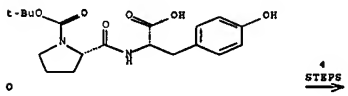
RX(41) OF 77 COMPOSED OF RX(2), RX(3), RX(4), RX(16)
RX(41) C + F + M + O ===> T



C F

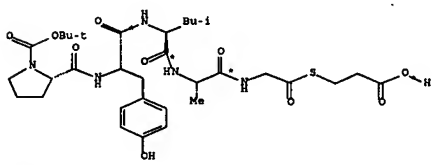


M



O

4 STEPS



T
YIELD 83%

RX(2) RCT C 503440-95-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO G 503440-96-8
NTE intermediate product could be isolated

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

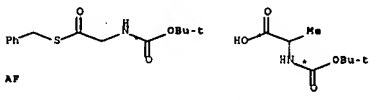
STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO P 503440-98-0
NTE intermediate product could be isolated

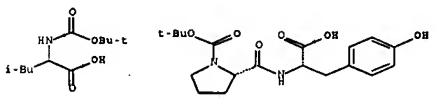
RX(16) RCT P 503440-98-0

RGT AP 64-19-7 AcOH, AQ 7440-66-6 Zn
PRO T 854749-15-8
SOL 64-19-7 AcOH, 7732-18-5 Water
CON 1 hour, room temperature

RX(48) OF 77 COMPOSED OF RX(11), RX(12), RX(15)
RX(48) AF + F + AJ + O ===> AL

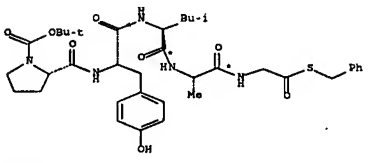


AF F



AJ O

3 STEPS



AL
YIELD 70%

RX(11) RCT AF 667905-05-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, AI 121-44-8 Et3N
SOL 109-99-9 THF
CON room temperature

STAGE(3)
RGT J 538-75-0 DCC
CON overnight, room temperature

PRO AH 667905-06-8
NTE intermediate product could be isolated

RX(12) RCT AH 667905-06-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT AJ 13139-15-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON 24 hours, room temperature

PRO AK 667905-07-9
NTE intermediate product could be isolated

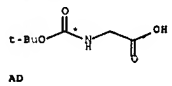
RX(15) RCT AK 667905-07-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

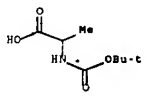
STAGE(2)
RCT O 132149-57-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON overnight, room temperature

PRO AL 667905-09-1
NTE intermediate product could be isolated

RX(49) OF 77 COMPOSED OF RX(10), RX(11), RX(12), RX(15)
RX(49) AD + AE + F + AJ + O ===> AL


AD


AE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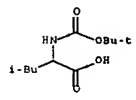
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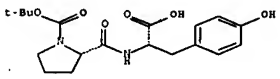
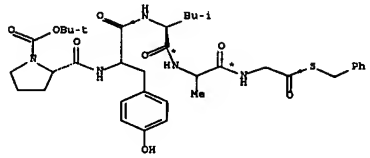

O

4 STEPS


AL
YIELD 70%

RX(10) RCT AD 4530-20-5, AE 100-53-8

STAGE(1)
RGT AG 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(2)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO AF 667905-05-7

RX(11) RCT AF 667905-05-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, AI 121-44-8 Et3N
SOL 109-99-9 THF
CON room temperature

STAGE(3)
RGT J 538-75-0 DCC
CON overnight, room temperature

PRO AH 667905-06-8
NTE intermediate product could be isolated

RX(12) RCT AH 667905-06-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT AJ 13139-15-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON 24 hours, room temperature

PRO AK 667905-07-9
NTE intermediate product could be isolated

RX(15) RCT AK 667905-07-9

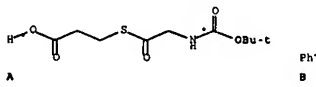
STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT S 165534-43-0 1,2,3-Benzotriazin-4(3H)-one, 3-[(diethoxyphosphinyl)oxy]-, AI 121-44-8 Et3N
SOL 68-12-2 DMF
CON overnight, room temperature

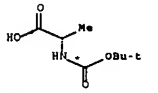
PRO AL 667905-09-1
NTE intermediate product could be isolated

RX(57) OF 77 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(16)

RX(57) A + B + F + M + O ===> T


A


B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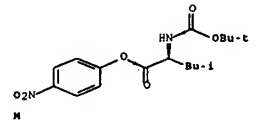
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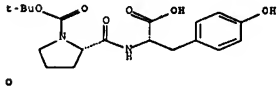
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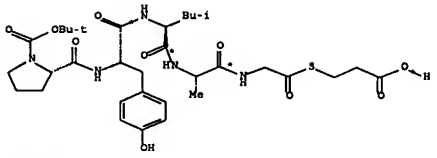
5 STEPS


T
YIELD 83%

RX(1) RCT A 133367-03-0, B 70-11-1
RGT D 7087-68-5 EtN(Pr-i)2
PRO C 503440-95-7
SOL 68-12-2 DMF

CON overnight, room temperature

RX(2) RCT C 503440-95-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO G 503440-96-8
NTE intermediate product could be isolated

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

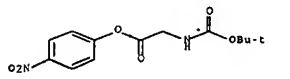
STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

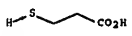
PRO P 503440-98-0
NTE intermediate product could be isolated

RX(16) RCT P 503440-98-0

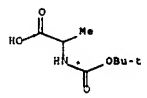
RGT AP 64-19-7 AcOH, AQ 7440-66-6 Zn
PRO T 854749-15-8
SOL 64-19-7 AcOH, 7732-18-5 Water
CON 1 hour, room temperature

RX(59) OF 77 COMPOSED OF RX(14), RX(1), RX(2), RX(3), RX(4)
RX(59) AN + AO + B + F + M + O ===>
P


AN


AO


B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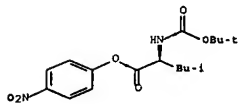
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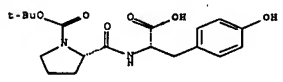
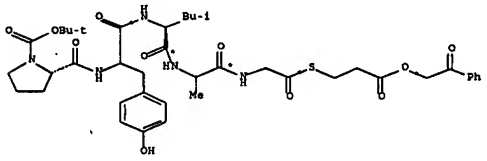

O

5 STEPS


P
YIELD 51%

RX(14) RCT AN 3655-05-8, AO 107-96-0
PRO A 133367-03-0
NTE literature prepn.

RX(1) RCT A 133367-03-0, B 70-11-1
RGT D 7087-68-5 EtN(Pr-i)2
PRO C 503440-95-7
SOL 68-12-2 DMF
CON overnight, room temperature

RX(2) RCT C 503440-95-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO G 503440-96-8
NTE intermediate product could be isolated

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

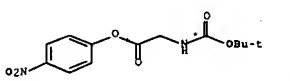
STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

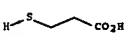
STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

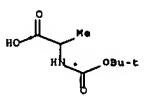
PRO P 503440-98-0
NTE intermediate product could be isolated

RX(61) OF 77 COMPOSED OF RX(14), RX(1), RX(2), RX(3), RX(4), RX(16)
RX(61) AN + AO + B + F + M + O ===>
T


AN


AO


B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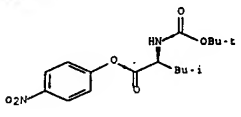

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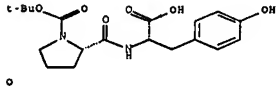
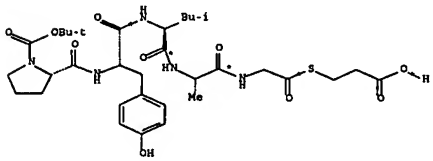


O

6 STEPS



T
YIELD 83%

RX(14) RCT AN 3655-05-8, AO 107-96-0
PRO A 133367-03-0
NTE literature prepn.

RX(1) RCT A 133367-03-0, B 70-11-1
RGT D 7087-68-5 EtN(Pr-i)2
PRO C 503440-95-7
SOL 68-12-2 DMF
CON overnight, room temperature

RX(2) RCT C 503440-95-7

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT F 15761-38-3

RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO G 503440-96-8
NTE intermediate product could be isolated

RX(3) RCT G 503440-96-8

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 20 minutes, room temperature

STAGE(2)
RCT M 3350-19-4
RGT D 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON 3 hours, room temperature, pH 8 - 9

PRO N 503440-97-9
NTE intermediate product could be isolated

RX(4) RCT N 503440-97-9

STAGE(1)
RGT H 7647-01-0 HCl
SOL 141-78-6 AcOEt
CON 15 minutes, room temperature

STAGE(2)
RCT O 132149-57-6
RGT I 2592-95-2 1-Benzotriazolol, D 7087-68-5 EtN(Pr-i)2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature, pH 7
SUBSTAGE(2) room temperature -> 0 deg C

STAGE(3)
RGT J 538-75-0 DCC
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) overnight, room temperature

PRO P 503440-98-0
NTE intermediate product could be isolated

RX(16) RCT P 503440-98-0
RGT AP 64-19-7 AcOH, AQ 7440-66-6 Zn
PRO T 854749-15-8
SOL 64-19-7 AcOH, 7732-18-5 Water
CON 1 hour, room temperature

L6 ANSWER 3 OF 28 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:89809 CASREACT Full-text
TITLE: Conversion of a Tyrosine Kinase Protein Substrate to a High Affinity Ligand by ATP Linkage
AUTHOR(S): Shen, Kui; Cole, Philip A.

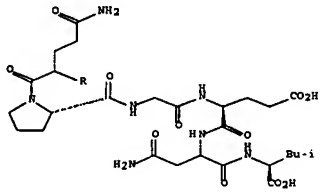
CORPORATE SOURCE: Department of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Journal of the American Chemical Society (2003), 125(52), 16172-16173
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protein kinases often show low affinity for their protein substrates, which makes it difficult to study kinase-substrate interactions. Here, the authors show using expressed protein ligation with the signaling protein Src that it is feasible to install a covalently linked ATP moiety into the tail of Src, generating a semisynthetic protein with a high affinity for its cognate tyrosine kinase, Csk. It is also established that this Src-ATP conjugate can be used to selectively pull down Csk from a complex protein mixture This work outlines a general strategy for identifying an unknown kinase that is responsible for the phosphorylation of a protein substrate on a site of interest.

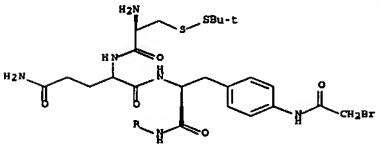
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 3 ...J + S ===> T

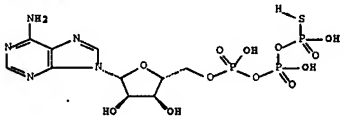
PAGE 1-A



PAGE 2-A



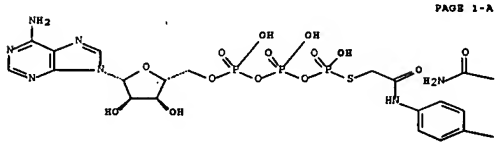
J



S

(2)

PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(2) RCT J 643760-37-6, S 35094-46-3

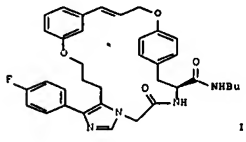
STAGE(1)
SOL 7732-18-5 Water
CON overnight, room temperature, pH 7

STAGE(2)
RGT U 3483-12-3 Cleland's reagent
SOL 7732-18-5 Water
CON 3 hours, room temperature, pH 7

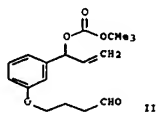
PRO T 643760-38-7
NTE Tris buffered soln. both stages, tris(2-carboxyethyl)phosphine alternately used in place of dithiothreitol

L6 ANSWER 4 OF 28 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:59928 CASREACT Full-text
TITLE: Methods to initiate synthetic re-structuring of peptides
AUTHOR(S): Wei, Qi; Harran, Susan; Harran, Patrick G.
CORPORATE SOURCE: Department of Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75390-9038, USA
SOURCE: Tetrahedron (2003), 59(45), 8947-8954
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



I

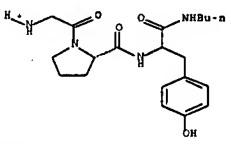


II

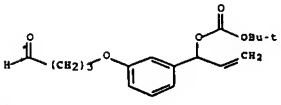
AB The authors present a protocol for the synthesis of macrocyclic peptide ethers via a multi-component condensation reaction followed by metal-catalyzed cycloetherification. For example, macrocycle I was obtained in two steps from the three-component condensation of reactants H-Gly-Tyr-NHBu, allyl carbonate II and isonitrile 4-FC6H4CH(N.tplbond.C)SO2C6H4Me-4, followed by cyclization of the adduct in presence of catalysts [(η3-allyl)PdCl]2 and van Leeuwen's Xantphos. The authors are currently studying the application of the above protocol to solid-phase synthesis.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

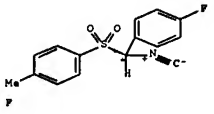
RX(24) OF 170 ...BM + B + F ===> R...



BM



B



F

(24)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

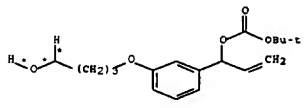
RX(24) RCT BM 639492-47-0, B 639491-67-1

STAGE(1)
RGT H 584-08-7 K2CO3
SOL 68-12-2 DMF
CON 5 hours, room temperature

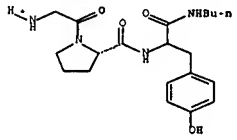
STAGE(2)
RCT F 165806-95-1
CON 17 hours, room temperature

PRO R 692740-58-2
NTE mol. sieve used in first stage

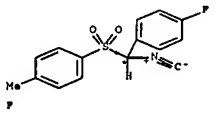
RX(35) OF 170 COMPOSED OF RX(1), RX(24)
RX(35) A + BM + F ===> R



A



BM



F

3 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(1) RCT A 692730-70-4
RGT C 110-86-1 Pyridine, D 87413-09-0 Martin's reagent
PRO B 639491-67-1
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 2 hours, room temperature

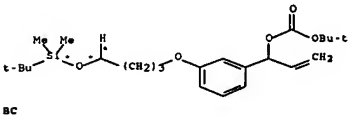
RX(24) RCT BM 639492-47-0, B 639491-67-1

STAGE(1)
RGT H 584-08-7 K2CO3
SOL 68-12-2 DMF
CON 5 hours, room temperature

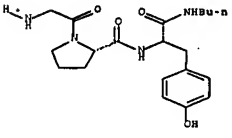
STAGE(2)
RCT F 165806-95-1
CON 17 hours, room temperature

PRO R 692740-58-2
NTE mol. sieve used in first stage

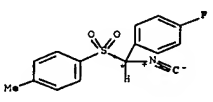
RX(96) OF 170 COMPOSED OF RX(20), RX(1), RX(24)
RX(96) BC + BM + F ===> R



BC



BM



F

3 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(20) RCT BC 692730-27-1
RGT C 110-86-1 Pyridine, BE 32001-55-1 4-MeOC6H4CPh2Cl
PRO A 692730-70-4
SOL 109-99-9 THF
CON 4 hours, room temperature

RX(1) RCT A 692730-70-4
RGT C 110-86-1 Pyridine, D 87413-09-0 Martin's reagent
PRO B 639491-67-1
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 2 hours, room temperature

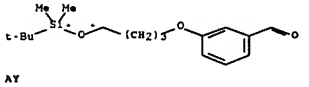
RX(24) RCT BM 639492-47-0, B 639491-67-1

STAGE(1)
RGT H 584-08-7 K2CO3
SOL 68-12-2 DMF
CON 5 hours, room temperature

STAGE(2)
RCT F 165806-95-1
CON 17 hours, room temperature

PRO R 692740-58-2
NTE mol. sieve used in first stage

RX(107) OF 170 COMPOSED OF RX(19), RX(20), RX(1), RX(24)
RX(107) AY + BA + BB + BM + F ===> R



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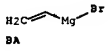

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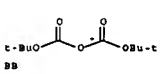

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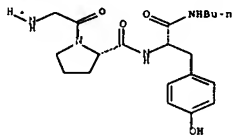
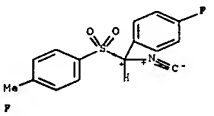


BM



F

4 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(19) RCT AY 692729-77-4, BA 1826-67-1

STAGE(1)
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -70 deg C
SUBSTAGE(2) 30 minutes, -70 deg C
SUBSTAGE(3) 45 minutes, -70 deg C -> room temperature

STAGE(2)
RCT BB 24424-99-5
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 20 minutes, room temperature
SUBSTAGE(2) 3.5 hours, room temperature

PRO BC 692730-27-1

RX(20) RCT BC 692730-27-1
RGT C 110-86-1 Pyridine, BE 32001-55-1 4-MeOC6H4CPh2Cl
PRO A 692730-70-4
SOL 109-99-9 THF
CON 4 hours, room temperature

RX(1) RCT A 692730-70-4
RGT C 110-86-1 Pyridine, D 87413-09-0 Martin's reagent
PRO B 639491-67-1
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 2 hours, room temperature

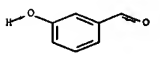
RX(24) RCT BM 639492-47-0, B 639491-67-1

STAGE(1)
RGT H 584-08-7 K2CO3
SOL 68-12-2 DMF
CON 5 hours, room temperature

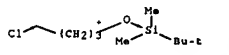
STAGE(2)
RCT F 165806-95-1
CON 17 hours, room temperature

PRO R 692740-58-2
NTE mol. sieve used in first stage

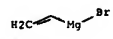
RX(139) OF 170 COMPOSED OF RX(18), RX(19), RX(20), RX(1), RX(24)
RX(139) AW + AX + BA + BB + BM + F ===> R



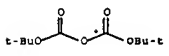
AW



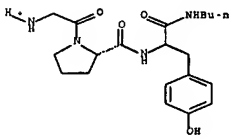
AX



BA



BB



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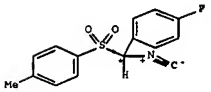


F

5 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(18) RCT AW 100-83-4, AX 89031-83-4
RGT AZ 534-17-8 Cs2CO3
PRO AY 692729-77-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) room temperature -> 115 deg C
SUBSTAGE(2) 4 hours, 115 deg C

SUBSTAGE(3) 1.5 hours, 115 deg C

RX(19) RCT AY 692729-77-4, BA 1826-67-1

STAGE(1)
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -70 deg C
SUBSTAGE(2) 30 minutes, -70 deg C
SUBSTAGE(3) 45 minutes, -70 deg C -> room temperature

STAGE(2)
RCT BB 24424-99-5
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 20 minutes, room temperature
SUBSTAGE(2) 3.5 hours, room temperature

PRO BC 692730-27-1

RX(20) RCT BC 692730-27-1
RGT C 110-86-1 Pyridine, BE 32001-55-1 4-MeOC6H4CPh2Cl
PRO A 692730-70-4
SOL 109-99-9 THF
CON 4 hours, room temperature

RX(1) RCT A 692730-70-4
RGT C 110-86-1 Pyridine, D 87413-09-0 Martin's reagent
PRO B 639491-67-1
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 2 hours, room temperature

RX(24) RCT BM 639492-47-0, B 639491-67-1

STAGE(1)
RGT H 584-08-7 K2CO3
SOL 68-12-2 DMF
CON 5 hours, room temperature

STAGE(2)
RCT F 165806-95-1
CON 17 hours, room temperature

PRO R 692740-58-2
NTE mol. sieve used in first stage

L6 ANSWER 5 OF 28 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:59920 CASREACT Full-text
TITLE: Synthesis of a functionalized high affinity mannose receptor ligand and its application in the construction of peptide-, polyamide- and PNA-conjugates
AUTHOR(S): Kinzel, Olaf; Fattori, Daniela; Ingallinella, Paolo; Bianchi, Elisabetta; Pessi, Antonello
CORPORATE SOURCE: Department of Molecular and Cell Biology, IRBM P. Angeletti, Pomezia, 00040, Italy
SOURCE: Journal of Peptide Science (2003), 9(6), 375-385
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of a high affinity mannose receptor ligand, appropriately functionalized for chemoselective ligation with an antigen or DNA-binding moieties is described. By a combination of solid- and solution-phase chemical a versatile synthesis of the target structure was accomplished. Examples of subsequent ligation reactions are described.

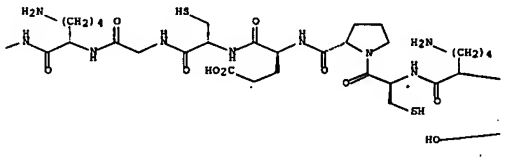
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(8) OF 73 AG ===> AH...

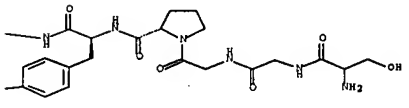
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

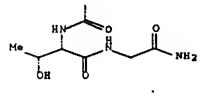
PAGE 1-C



PAGE 1-D



PAGE 2-A



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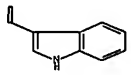

AG

(8)

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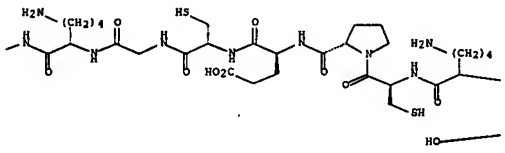
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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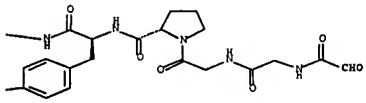

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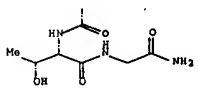

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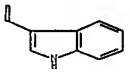


AH
YIELD 58%

RX(8) RCT AG 635708-52-0

STAGE(1)
RGT AI 7646-85-7 ZnCl2, AJ 7558-79-4 Na2HPO4, AK 63-68-3 L-Methionine, AL 7790-28-5 NaIO4
SOL 7732-18-5 Water
CON 15 minutes, room temperature

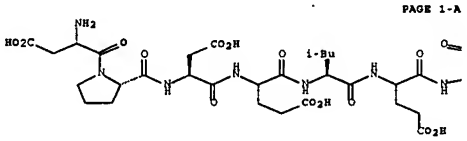
STAGE(2)
RGT O 76-05-1 F3CCO2H

PRO AH 635708-53-1

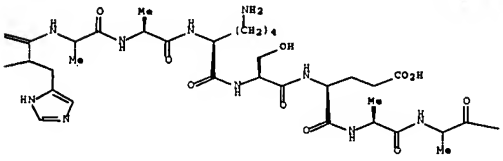
L6 ANSWER 6 OF 28 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 139:214703 CASREACT Full-text
TITLE: Synthesis and hydrolysis studies of a peptide containing the reactive triad of serine proteases with an associated linker to a dye on a solid phase support
AUTHOR(S): Clough, John M.; Jones, Ray V. H.; McCann, Hannah; Morris, David J.; Wills, Martin
CORPORATE SOURCE: Syngenta, Jealott's Hill Research Centre, Berkshire, RG42 6EY, UK
SOURCE: Organic & Biomolecular Chemistry (2003), 1(9), 1486-1497
CODEN: OBCRAK; ISSN: 1477-0520
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of a Tentagel-supported peptide incorporating the reactive triad of serine, histidine and aspartic acid, found within serine protease enzymes, is described.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(35) OF 256 ...BN + AK ===> BO

PAGE 1-A



PAGE 1-B



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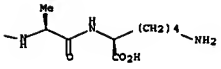
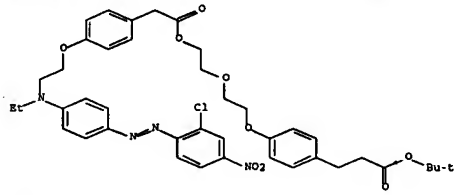


BN
resin-bound



AK

(35)

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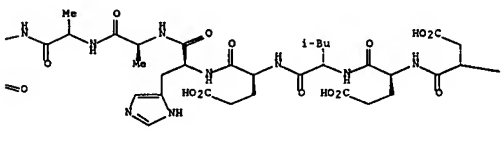
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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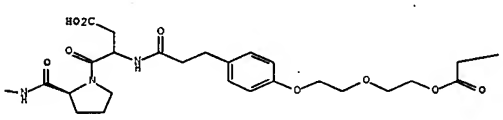
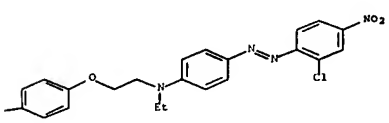


PAGE 1-D



PAGE 2-A

BO
resin-bound

RX(35) RCT BN 590402-32-7D, AK 590402-17-8

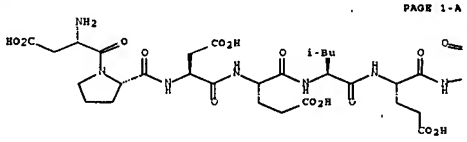
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5
EtN(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane,
tris(1-methylethyl)-
CON 2 hours, room temperature

PRO BO 590402-41-8D
NTE solid-supported reaction, first stage attachment to resin

RX(36) OF 256 ...BN + AL ===> BS

PAGE 1-A



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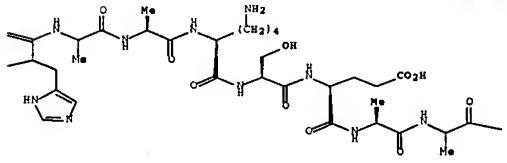

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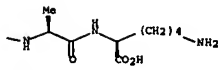
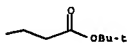


BN
resin-bound

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

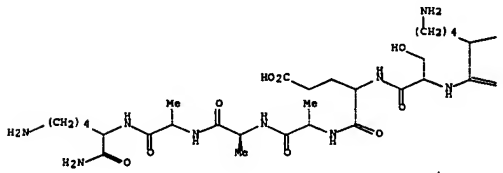
PAGE 1-B



AL

(36)

PAGE 1-A



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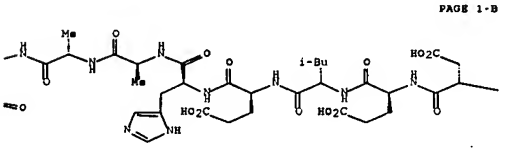
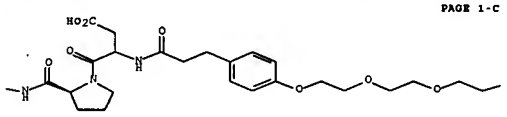


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(36) RCT BN 590402-32-7D, AL 590402-19-0

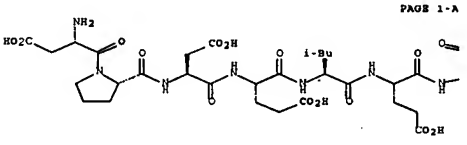
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5
EtN(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane,
tris(1-methylethyl)-
CON 2 hours, room temperature

PRO BS 590402-42-9D
NTE solid-supported reaction, first stage attachment to resin

RX(37) OF 256 ...BN + AM ===> BT

PAGE 1-A



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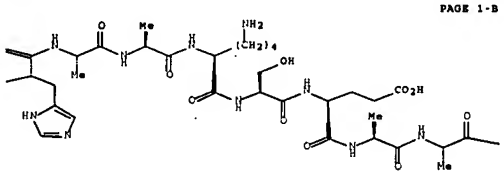

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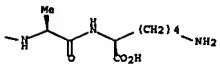
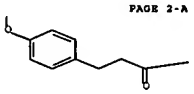


BN
resin-bound

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



PAGE 2-B

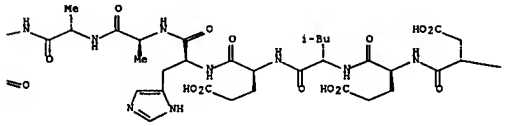
—OBu-t

AM

(37)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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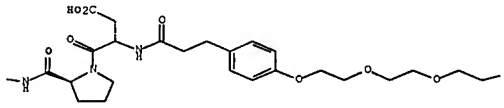

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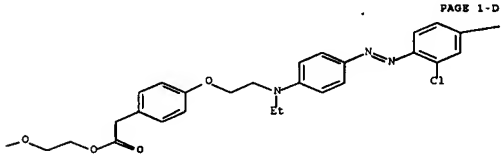


PAGE 1-E

—NO2

PAGE 2-A

BT
resin-bound

RX(37) RCT BN 590402-32-7D, AM 590402-21-4

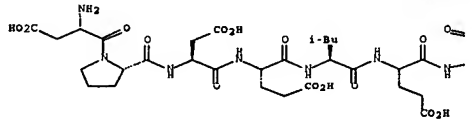
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5 Et3N(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane, tris(1-methylethyl)-
CON 2 hours, room temperature

PRO BT 590402-43-0D
NTE solid-supported reaction, first stage attachment to resin

RX(38) OF 256 ...BN + AN ===> BU

PAGE 1-A



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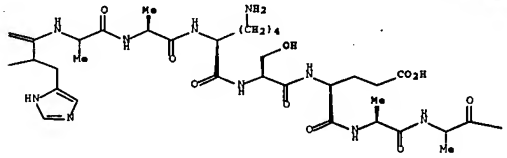

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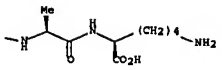
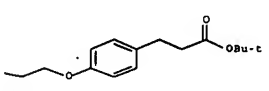


BN
resin-bound

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

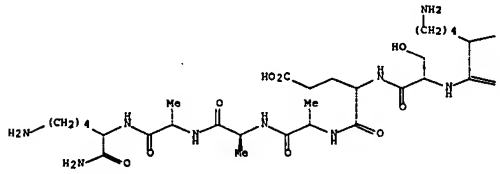
PAGE 1-B



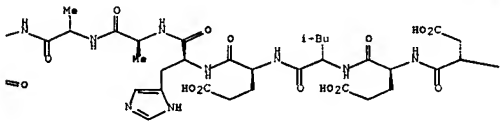
AN

(38)

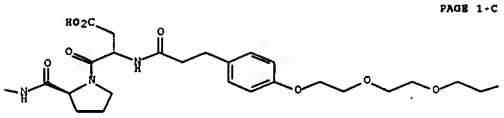
PAGE 1-A



PAGE 1-B



PAGE 1-C



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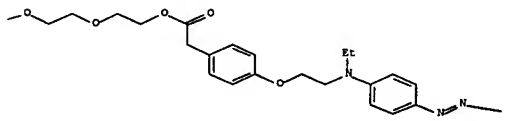


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(38) RCT BN 590402-32-7D, AN 590402-23-6

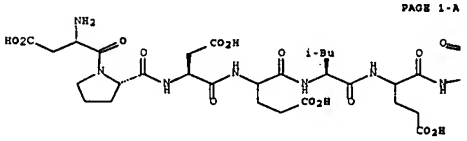
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5
EtN(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane,
tris(1-methylethyl)-
CON 2 hours, room temperature

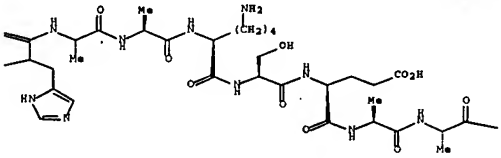
PRO BU 590402-44-1D
NTE solid-supported reaction, first stage attachment to resin

RX(39) OF 256 ...BN + AO ===> BV

PAGE 1-A



PAGE 1-B



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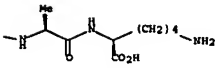
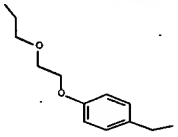


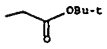
BN
resin-bound

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



PAGE 2-B

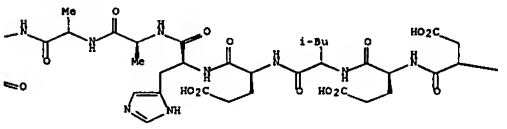


AO

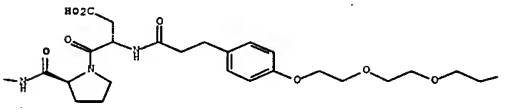
(39)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 1-C



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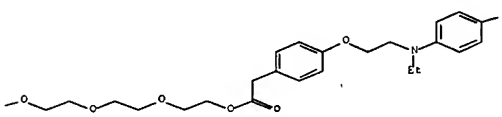

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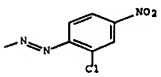


PAGE 2-A

BV
resin-bound

RX(39) RCT BN 590402-32-7D, AO 590402-25-8

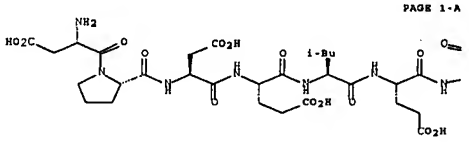
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5
EtN(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane,
tris(1-methylethyl)-
CON 2 hours, room temperature

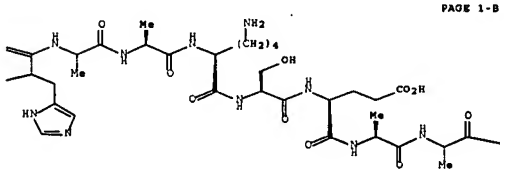
PRO BV 590402-45-2D
NTE solid-supported reaction, first stage attachment to resin

RX(40) OF 256 ...BN + AP ===> BW

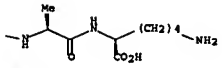
PAGE 1-A



PAGE 1-B



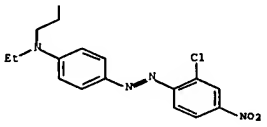
PAGE 1-C



BN
resin-bound

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

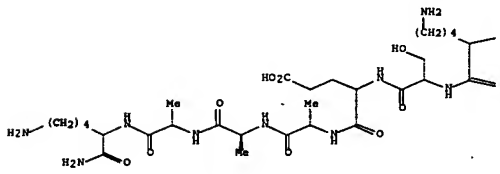
PAGE 2-A



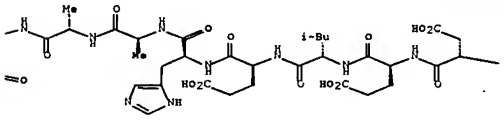
AP

(40)

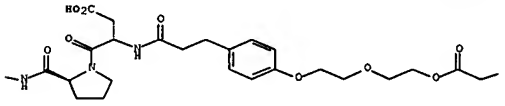
PAGE 1-A



PAGE 1-B



PAGE 1-C



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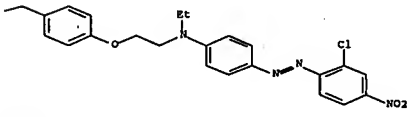


BN
resin-bound

RX(40) RCT BN 590402-32-7D, AP 590402-26-9

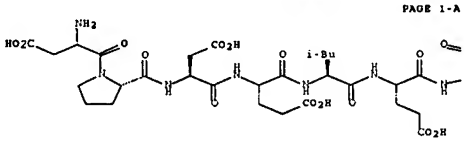
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5
EtN(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane,
tris(1-methylethyl)-
CON 2 hours, room temperature

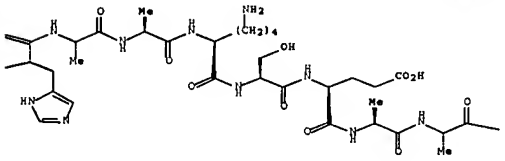
PRO BW 590402-46-3D
NTE solid-supported reaction, first stage attachment to resin

RX(41) OF 256 ...EN + AQ ===> BX

PAGE 1-A



PAGE 1-B



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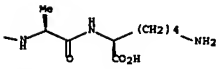
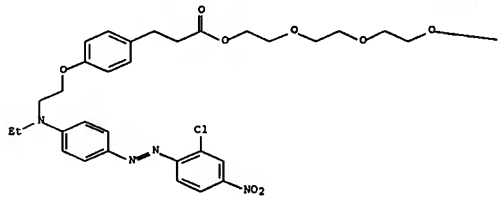
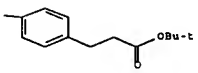


BN
resin-bound

PAGE 1-A



PAGE 1-B

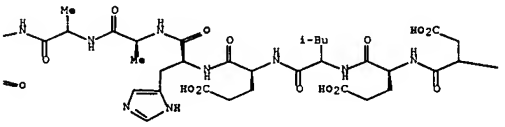


AQ

(41)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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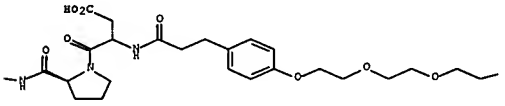

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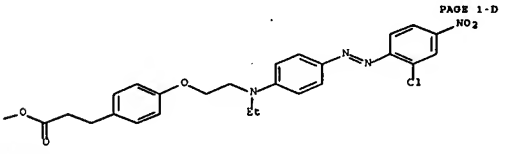


BX
resin-bound

RX(41) RCT BN 590402-32-7D, AQ 590402-27-0

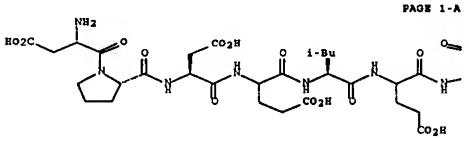
STAGE(1)
RGT BP 128625-52-5 Benzotriazolol P der, BQ 7087-68-5 EtN(Pr-i)2, BR 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF
CON 3 hours, room temperature

STAGE(2)
RGT AV 76-05-1 F3CCO2H, AW 6485-79-6 Silane, tris(1-methylethyl)-
CON 2 hours, room temperature

PRO BX 590402-47-4D
NTE solid-supported reaction, first stage attachment to resin

RX(42) OF 256 ...BN + AR ===> BY

PAGE 1-A



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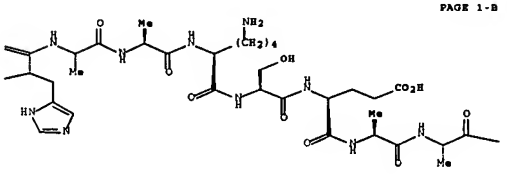

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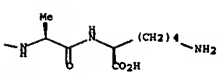

BN
resin-bound

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B

OBu-t

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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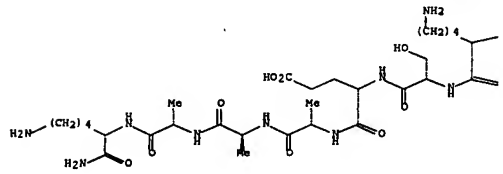
PAGE 1-A



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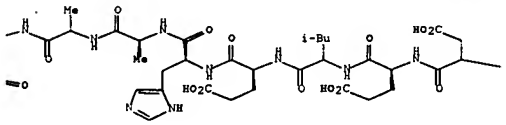

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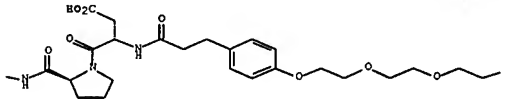
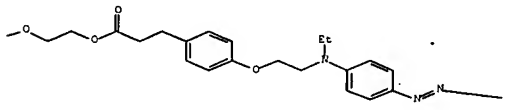


PAGE 1-D



<------User Break------>

=>

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 5.52 130.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE 0.00 -0.73

FILE 'REGISTRY' ENTERED AT 08:28:44 ON 30 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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provided by InfoChem.

STRUCTURE FILE UPDATES: 28 MAY 2007 HIGHEST RN 935999-19-2
DICTIONARY FILE UPDATES: 28 MAY 2007 HIGHEST RN 935999-19-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
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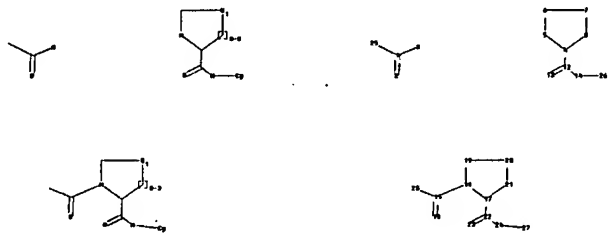
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10.561754\clm14 crop1 plus.str



chain nodes :
1 2 3 12 13 14 15 16 22 23 24 25 26 27 28

ring nodes :
4 5 6 7 8 17 18 19 20 21
chain bonds :
1-3 1-2 1-25 4-12 12-13 12-14 14-26 15-18 15-16 15-28 17-22 22-23 22-24
24-27
ring bonds :
4-5 4-8 5-6 6-7 7-8 17-18 17-21 18-19 19-20 20-21
exact/norm bonds :
1-3 1-2 1-25 4-5 4-8 4-12 5-6 6-7 7-8 12-13 12-14 14-26 15-18 15-16
15-28 17-18 17-21 17-22 18-19 19-20 20-21 22-23 22-24 24-27

G1:C,S

Match level :
1:CLASS 2:CLASS 3:CLASS 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 12:CLASS 13:CLASS
14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:CLASS 23:CLASS
24:CLASS 25:CLASS 26:Atom 27:Atom 28:CLASS
fragments assigned product role:
containing 15
fragments assigned reactant/reagent role:
containing 1
containing 4

L7 STRUCTURE UPLOADED

=> d
L7 HAS NO ANSWERS
L7 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> file casreact
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.45 130.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE 0.00 -0.73

FILE 'CASREACT' ENTERED AT 08:29:13 ON 30 MAY 2007
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FILE CONTENT:1840 - 27 May 2007 VOL 146 ISS 23

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
* *
* CASREACT now has more than 12 million reactions *

Soma CASREACT racords ara derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compilad under tha direction of Professor Dr. Klaus Kieslich.

This file contains CAS Ragistry Numbers for easy and accurata substanca identification.

=> s l7
SAMPLE SEARCH INITIATED 08:29:18 FILE 'CASREACT'
SCREENING COMPLETE - 1444 REACTIONS TO VERIFY FROM 71 DOCUMENTS

100.0% DONE 1444 VERIFIED 20 HIT RXNS 5 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 26603 TO 31157
PROJECTED ANSWERS: 5 TO 234

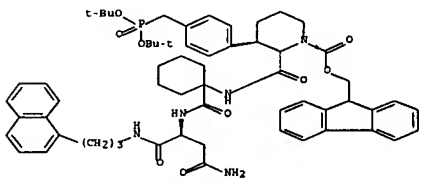
L8 5 SEA SSS SAM L7 (20 REACTIONS)

=> s l8 not py > 2003
101431 PY > 2003
L9 3 L8 NOT PY > 2003

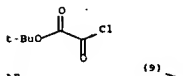
=> d ibib abs fhit

L9 ANSWER 1 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:385710 CASREACT Full-text
TITLE: Synthesis of N-Fmoc 3-[4-(di-tert-butylphosphonomethyl)phenyl]pipecolic acid as a conformationally constrained phosphotyrosyl mimetic suitably protected for peptida synthesis
AUTHOR(S): Liu, Ding-Guo; Wang, Xiang-Zhu; Gao, Yang; Li, Bihua; Yang, Dajun; Burke, Terrence R.
CORPORATE SOURCE: Center for Cancer Research, Laboratory of Medicinal Chamistry, NCI at Fraderick, Frederick, MD, 21702, USA
SOURCE: Tetrahedron (2002), 58(52), 10423-10428
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsaviar Scianca Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phosphonomethylphanylalanine (Pmp) has shown wide utility as a hydrolytically stable phosphotyrosyl mimetic, particularly in Src homol. 2 (SH2) domain-binding peptides. (2S,3R)-3-[4-(phosphonomathyl)phenyl]pipac olic acid (3) raprasents a variant of Pmp having ϕ and $\chi 1$ torsion angles constrained through incorporation into the piperidinyl ring structure contained within pipecolic acid. Raported hara is tha anantioselactiva preparation of 3, in an orthogonally protected form (title compound, 4) suitabla for usa in peptide synthesis. Stereochemistries at both the 2- and 3-positions are derived inductivaly from a single chiral center provided by the com. available Evans chiral auxiliary, (4S)-4-banzyl-1,3-oxazolidin-2-ona. Incorporation of 4 into a Grb2 SH2 domain-directed tripeptide showed that Grb2 SH2 domain-binding affinity was raducad ralativa to the parent Pmp-containing tripeptide. Although conformational constraint did not enhance affinity in this case, novel amino acid analog 4 may serve as a useful tool for the induction of dafinad phosphotyrosyl geometry in peptides directed at other signal transduction targets.

RX(9) OF 55 ...J + AP ===> AQ...

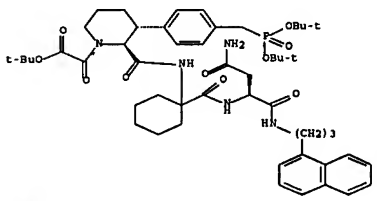


J



AP

(9)



AQ
YIELD 77%

RX(9) RCT J 525575-18-2

STAGE(1)
RGT AR 110-89-4 Piperidina
SOL 75-05-8 MeCN
CON 4 hours, room temperature

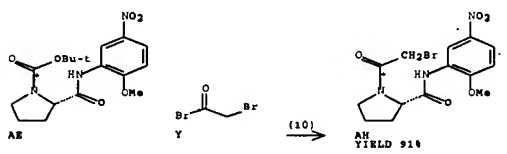
STAGE(2)
RCT AP 39061-59-1
RGT AS 7087-68-5 EtN(Pr-i)2
SOL 68-12-2 DMF
CON overnight, room temperature

PRO AQ 525575-19-3
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>
=> d ibib abs fhit 2-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 2 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:247666 CASREACT Full-text
TITLE: Bicyclic piperazinylbenzenasulphonamides are potent and selective 5-HT6 receptor antagonists
AUTHOR(S): Bromidge, Steven M.; Clarke, Stephan E.; King, Frank D.; Lovell, Peter J.; Newman, Helen; Riley, Graham; Routledge, Carol; Serafinowska, Halina T.; Smith, Douglas R.; Thomas, David R.
CORPORATE SOURCE: Department of Psychiatry, GlaxoSmithKline, Essex, Harlow, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(10), 1357-1360
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of novel 3-(octahydropyrido[1,2-a]pyrazin-2-yl)- and 3-(hexahydropyrrolo[1,2-a]pyrazin-2-yl)phenyl-2-benzo[b]thiophene sulfonamide derivs. is described. The compds. show high affinity for the 5-HT6 receptor, excellent salactivity against a range of other receptors, and good brain penatration.

RX(10) OF 33 ...AE + Y ===> AH...



AE Y AH
(10)
YIELD 91%

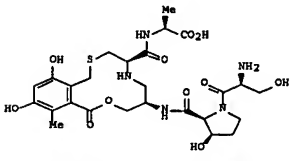
RX(10) RCT AE 239122-42-0

STAGE(1)
RGT AI 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

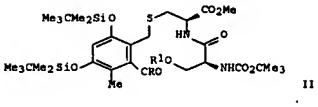
STAGE(2)
RCT Y 598-21-0
RGT D 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2

PRO AH 239122-44-2
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 126:116191 CASREACT Full-text
TITLE: Total synthesis of cyclothialidine
AUTHOR(S): Goetschi, Erwin; Jenny, Christian Johannes; Reindl, Peter; Ricklin, Fabianne
CORPORATE SOURCE: Pharma Division, Hoffmann-La Rocha Ltd., Basel, CH-4002, Switz.
SOURCE: Helvatica Chimica Acta (1996), 79(8), 2219-2234
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



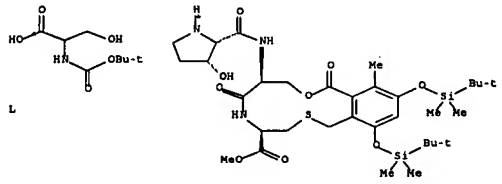
I



II

AB A total synthesis of cyclothialidine I, a DNA gyrasa inhibitor isolated from Streptomyces filipinensis, is described. The synthetic concept was tested by preparing a lactone containing the bicyclic core entity of I. Key features of the synthesis of I are preparation of 3,5-dihydroxy-2,6- dimathylbenzoate from 3,5-dihydroxybenzoate by 2 consecutive Mannich aminomathylation/hydroganation saquencas, benzylic N-bromosuccinimide bromination of an ester derivative thereof and its subsequent coupling with Boc-Sar-Cys-OMe, cyclization of tha ω-hydroxy acid II (R = OH, R1 = H) to the 12-membered lactone II (RR1 = bond) using praferably Mitsunobu conditions, and complation of the peptidic side chains of I using Boc strategy. Optically pure cis-N-(tert-butoxycarbonyl)-3-hydroxy-L-proline was obtained by rasolution of tha racemata via an efficient raaction saquanca containing a lipasa-catalyzad enantiospacific acatata hydrolysis. Tha structura of natural I was confirmad by comparison with tha synthatic matarial. The synthetic route described provides also easy accass to analogs of I.

RX(5) OF 433 ...L + P ===> Q...



L

P

(5)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

YIELD 73%

RX(5) RCT L 3262-72-4, P 186132-90-1
RGT R 25952-53-8 EDAP
PRO Q 186132-91-2
SOL 75-05-8 MeCN

=>
=> d hist

(FILE 'HOME' ENTERED AT 08:18:24 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 08:18:37 ON 30 MAY 2007
L1 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:19:13 ON 30 MAY 2007
L2 0 S L1 SSS SAM
L3 1 S L1 SSS FULL

FILE 'REGISTRY' ENTERED AT 08:21:37 ON 30 MAY 2007

L4 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:21:56 ON 30 MAY 2007
L5 50 S L4

FILE 'CASREACT' ENTERED AT 08:24:06 ON 30 MAY 2007
L6 28 S L5 NOT PY>2003

FILE 'REGISTRY' ENTERED AT 08:28:44 ON 30 MAY 2007
L7 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:29:13 ON 30 MAY 2007
L8 5 S L7
L9 3 S L8 NOT PY > 2003

=> s l7 sss full
FULL SEARCH INITIATED 08:47:17 FILE 'CASREACT'
SCREENING COMPLETE - 30569 REACTIONS TO VERIFY FROM 1466 DOCUMENTS

100.0% DONE . 30569 VERIFIED 455 HIT RXNS 46 DOCS
SEARCH TIME: 00.00.04

L10 46 SEA SSS FUL L7 (455 REACTIONS)

=> s l10 not py >2003
101431 PY >2003
L11 21 L10 NOT PY >2003

=> s l11 not l9
L12 18 L11 NOT L9

=> d ibib abs hit 1-10

L12 ANSWER 1 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:447413 CASREACT Full-text
TITLE: Preparation of tripeptides as hepatitis C virus inhibitors
PATENT ASSIGNEE(S): Boehringer Ingelheim Canada Ltd., Can.
SOURCE: Can. Pat. Appl., 33 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2370400	A1	20030801	CA 2002-2370400	20020201

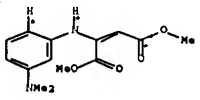
PRIORITY APPLN. INFO.: CA 2002-2370400 20020201
OTHER SOURCE(S): MARPAT 142:447413
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

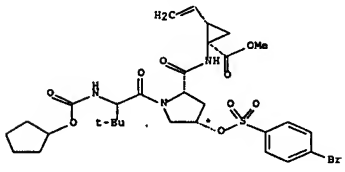
AB The invention relates to tripeptides I [B is H, (un)substituted aryl, aralkyl, heterocyclyl, acyl, CO2H or ester, a (thio)amide or sulfonyl group; Y is H or alkyl; R3 is (un)substituted alkyl, cycloalkyl or alkylcycloalkyl; R2 is CH2R20, NHR20, OR20 or SR20, where R20 is (un)substituted (un)saturated cycloalkyl, aryl, aralkyl, heterocyclyl, etc.; R1 is H, (un)substituted alkyl, cycloalkyl, alkenyl or alkynyl optionally substituted by

halogen] or their pharmaceutically-acceptable salts or esters, including racemates, diastereoisomers and optical isomers, which are inhibitors of the hepatitis C virus (HCV). Thus, tripeptide II was prepared by a multistep synthesis involving etherification of tripeptide prolinol derivative and cyclization of 2-(bromoacetyl)quinoline derivative with tert-butylacetylthiourea as key steps. Compound II is extremely active against the HCV NS3 protease on the basis of enzymic and cellular assays.

RX(11) OF 55 COMPOSED OF RX(2), RX(4)
RX(11) C + L ===> P

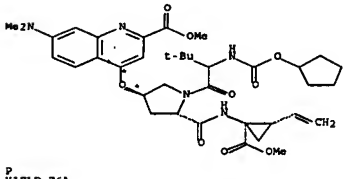


C



L

2 STEPS

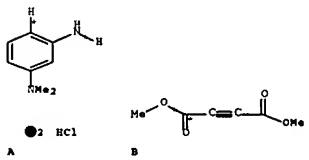


P
YIELD 76%

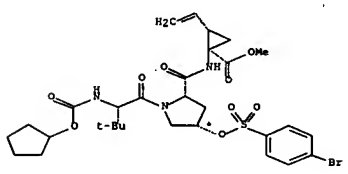
RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(18) OF 55 COMPOSED OF RX(1), RX(2), RX(4)
RX(18) A + B + L ===> P

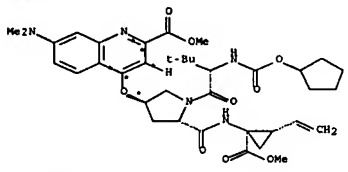


A B



L

3 STEPS



P
YIELD 76%

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

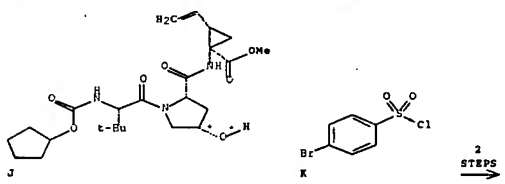
STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

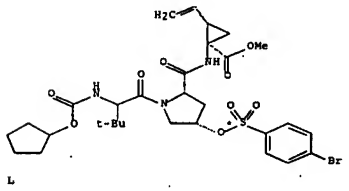
RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(19) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4)
AND REACTION SEQUENCE RX(2), RX(4)
...J + K ===> L...
... C + L ===> P

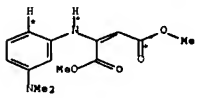


J K 2 STEPS

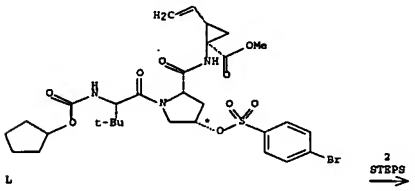


L

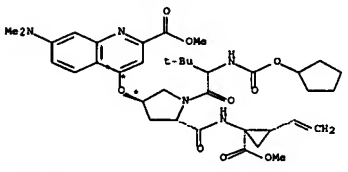
START NEXT REACTION SEQUENCE



C



L 2 STEPS



P
YIELD 76%

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

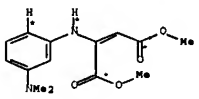
PRO L 801282-34-8

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two

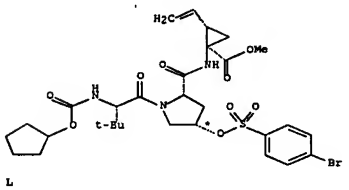
batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(20) OF 55 COMPOSED OF RX(2), RX(4), RX(5)
RX(20) C + L ===> S



C



L 3 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

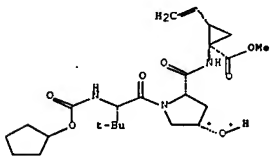
RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

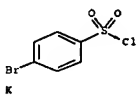
RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3

PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

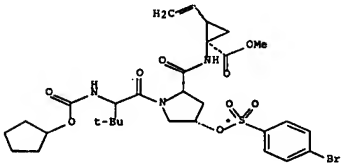
RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(21) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4)
AND REACTION SEQUENCE RX(1), RX(2), RX(4)
...J + K ===> L...
...A + B + L ===> P

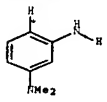

J

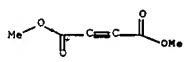

K

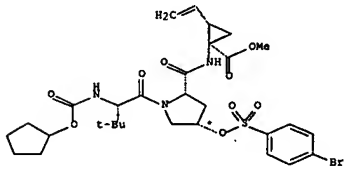
3 STEPS


L

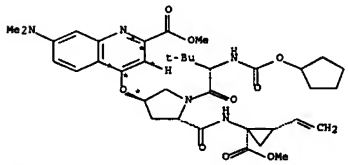
START NEXT REACTION SEQUENCE


●2 HCl
A


B


L

3 STEPS


P
YIELD 76%

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

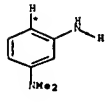
STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

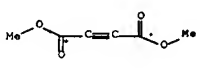
PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

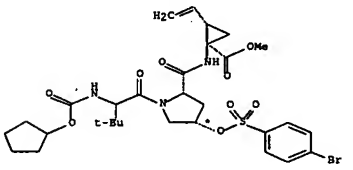
RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(22) OF 55 COMPOSED OF RX(1), RX(2), RX(4), RX(5)
RX(22) A + B + L ===> S


●2 HCl
A


B


L

4 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

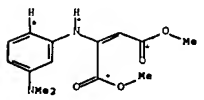
PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

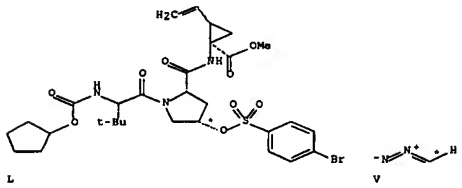
RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(25) OF 55 COMPOSED OF RX(2), RX(4), RX(5), RX(6)
RX(25) C + L + V ===> W



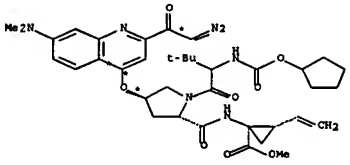
C



L

V

4 STEPS



W
YIELD 100%

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

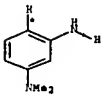
RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

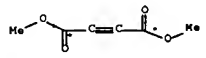
PRO W 851009-70-6

RX(33) OF 55 COMPOSED OF RX(1), RX(2), RX(4), RX(5), RX(6)
RX(33) A + B + L + V ===> W

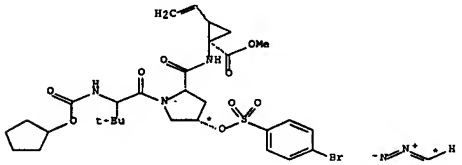


●2 HCl

A



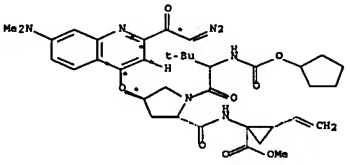
B



L

V

5 STEPS



W
YIELD 100%

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh

CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

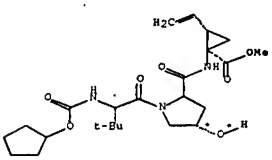
RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

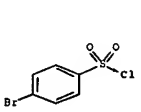
STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(34) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5)
AND REACTION SEQUENCE RX(2), RX(4), RX(5)
...J + K ===> L...
... C + L ===> S

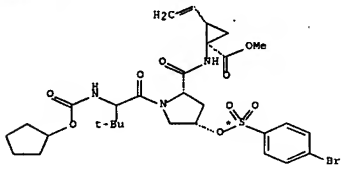


J



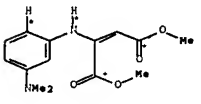
K

3 STEPS

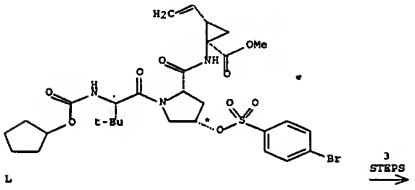


L

START NEXT REACTION SEQUENCE



C



L

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

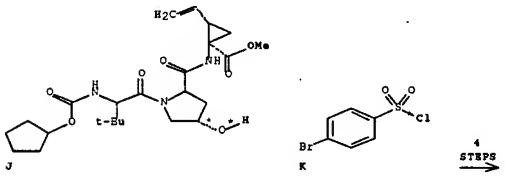
PRO L 801282-34-8

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

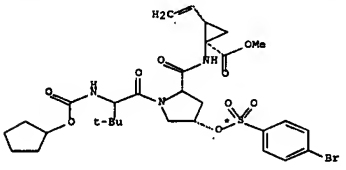
RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(35) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6) AND REACTION SEQUENCE RX(2), RX(4), RX(5), RX(6)
...J + K ===> L...
... C + L + V ===> W

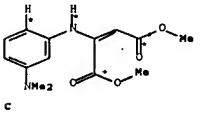


J K

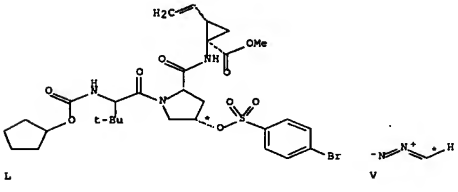


L

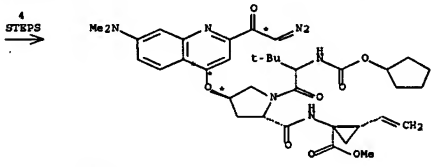
START NEXT REACTION SEQUENCE



C



L V



W
YIELD 100%

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

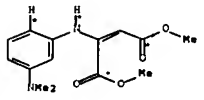
STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i

SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

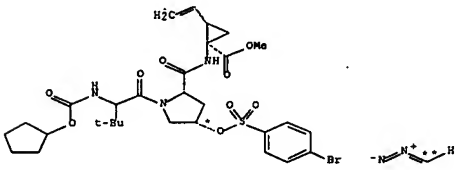
STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(36) OF 55 COMPOSED OF RX(2), RX(4), RX(5), RX(6), RX(7)
RX(36) C + L + V ===> Z

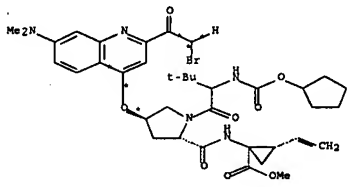


C



L V

5 STEPS



Z
YIELD 100%

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

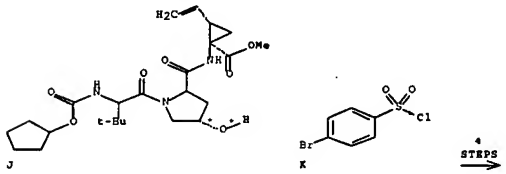
RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

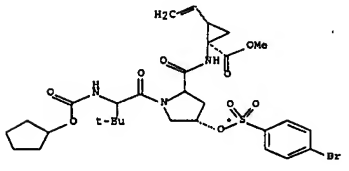
PRO Z 851009-71-7

RX(37) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5)
AND REACTION SEQUENCE RX(1), RX(2), RX(4), RX(5)
...J + K ===> L...
...A + B + L ===> S



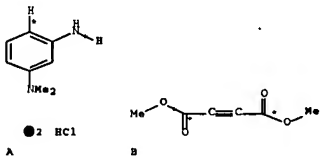
J K

4 STEPS



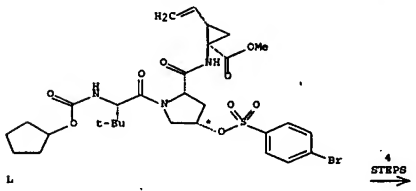
L

START NEXT REACTION SEQUENCE



●2 HCl

A B



L

4 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-56-6

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)

RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

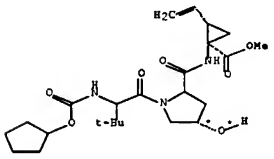
PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

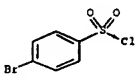
RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(38) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6)
AND REACTION SEQUENCE RX(1), RX(2), RX(4), RX(5), RX(6)
...J + K ===> L...
...A + B + L + V ===> W

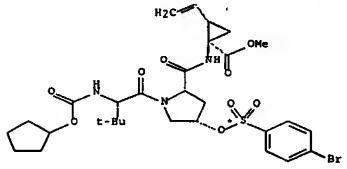


J



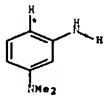
K

5 STEPS

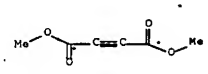


L

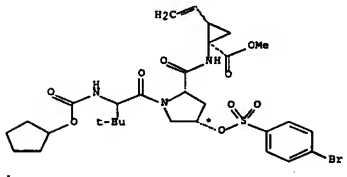
START NEXT REACTION SEQUENCE



●2 HCl
A



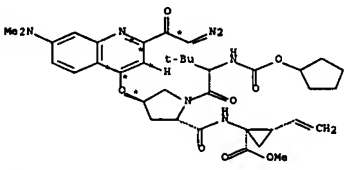
B



L

V

5 STEPS



W
YIELD 100%

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two

batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

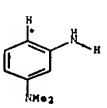
RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

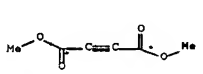
STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

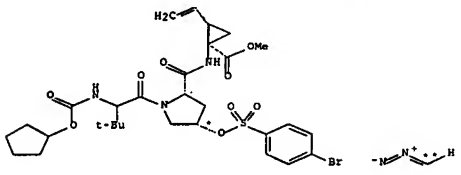
RX(39) OF 55 COMPOSED OF RX(1), RX(2), RX(4), RX(5), RX(6), RX(7)
RX(39) A + B + L + V ===> Z



●2 HCl
A

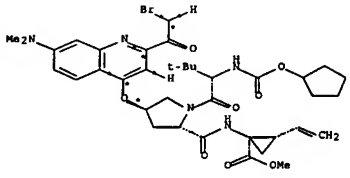


B



L V

6 STEPS



Z
YIELD 100%

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

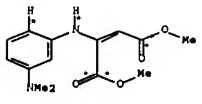
RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

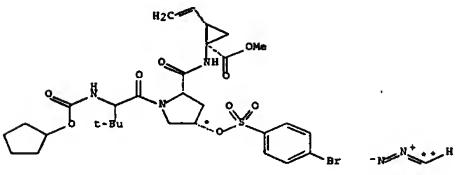
STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

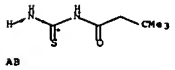
RX(42) OF 55 COMPOSED OF RX(2), RX(4), RX(5), RX(6), RX(7), RX(8)
RX(42) C + L + V + AB ===> AC



C

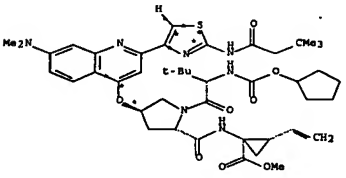


L V



AB

6 STEPS



AC

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

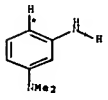
STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours

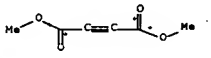
NTE overall yield over 4 steps is 53%

RX(44) OF 55 COMPOSED OF RX(1), RX(2), RX(4), RX(5), RX(6), RX(7), RX(8)
RX(44) A + B + L + V + AB ===> AC

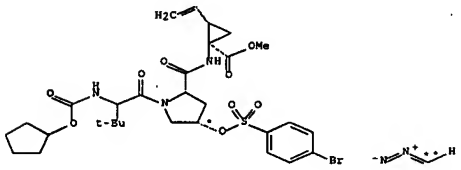


●2 HCl

A

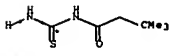


B



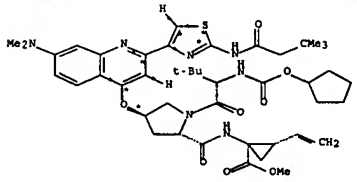
L

V



AB

7 STEPS →



AC

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degrees celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

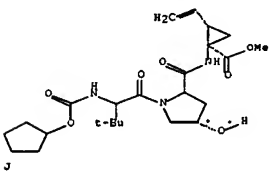
STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

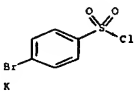
PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

RX(45) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6), RX(7)
AND REACTION SEQUENCE RX(2), RX(4), RX(5), RX(6), RX(7)
...J + K ===> L...
... C + L + V ===> Z

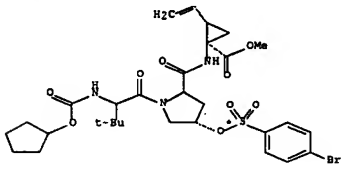


J



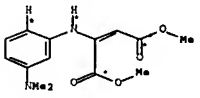
K

5 STEPS →

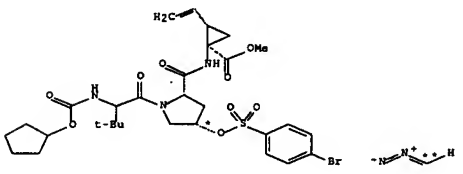


L

START NEXT REACTION SEQUENCE



C



L

V

5 STEPS →

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

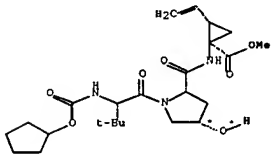
STAGE(1)

RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

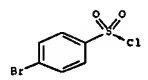
STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

RX(46) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6), RX(7), RX(8)
AND REACTION SEQUENCE RX(2), RX(4), RX(5), RX(6), RX(7), RX(8)
...J + K ===> L...
... C + L + V + AB ===> AC

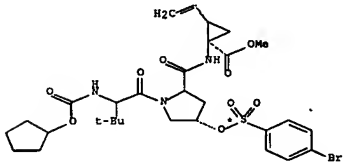


J



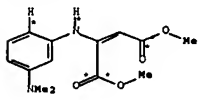
K

6 STEPS



L

START NEXT REACTION SEQUENCE



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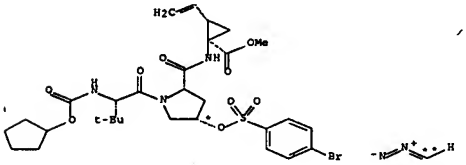
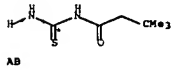


L

V



AB

6 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

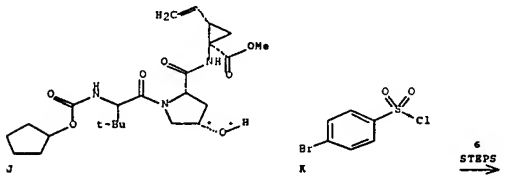
STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

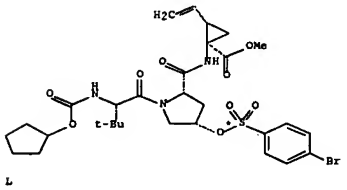
STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

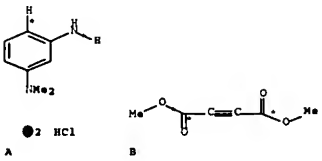
RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

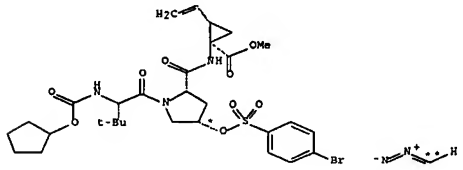
RX(47) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6), RX(7)
AND REACTION SEQUENCE RX(1), RX(2), RX(4), RX(5), RX(6), RX(7)
...J + K ===> L...
...A + B + L + V ===> Z





START NEXT REACTION SEQUENCE





* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5

NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8,Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

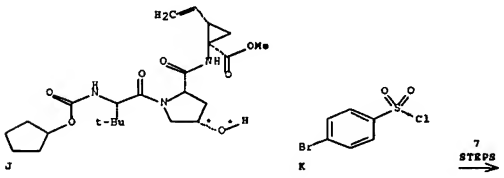
STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

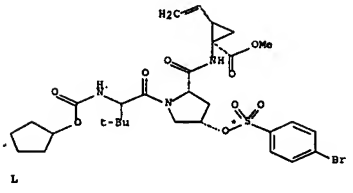
STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

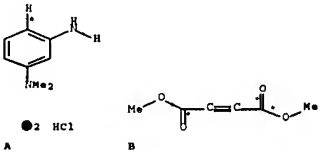
RX(48) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6), RX(7),
RX(8)

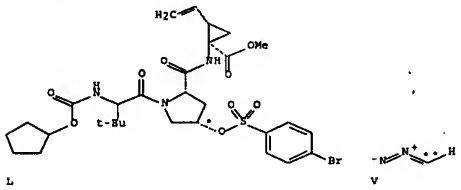
AND REACTION SEQUENCE RX(1), RX(2), RX(4), RX(5), RX(6), RX(7),
RX(8)
...J + K ===> L...
...A + B + L + V + AB. ===> AC



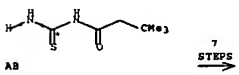


START NEXT REACTION SEQUENCE





L V



AB

7 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C

SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

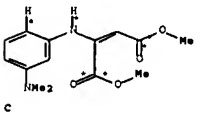
STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

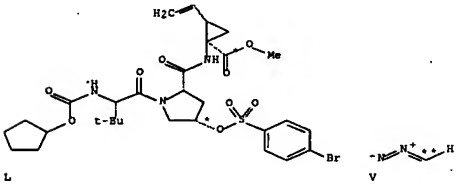
PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

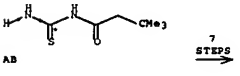
RX(51) OF 55 COMPOSED OF RX(2), RX(4), RX(5), RX(6), RX(7), RX(8), RX(9)
RX(51) C + L + V + AB ===> AB



C



L V



AB

7 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C

SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

RX(9) RCT AC 851009-72-8

STAGE(1)

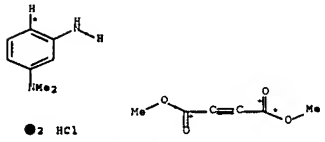
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, room temperature

STAGE(2)
RGT AF 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 6

STAGE(3)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON 15 minutes, room temperature

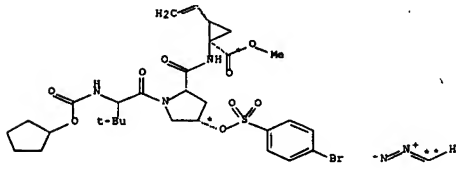
PRO AE 851009-74-0

RX(52) OF 55 COMPOSED OF RX(1), RX(2), RX(4), RX(5), RX(6), RX(7), RX(8), RX(9)
RX(52) A + B + L + V + AB ===> AE



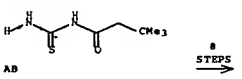
A

B



L

V



AB

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 601282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF

CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

RX(9) RCT AC 851009-72-8

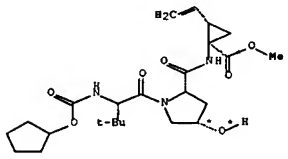
STAGE(1)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, room temperature

STAGE(2)
RGT AF 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 6

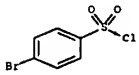
STAGE(3)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON 15 minutes, room temperature

PRO AE 851009-74-0

RX(54) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6), RX(7), RX(8), RX(9)
AND REACTION SEQUENCE RX(2), RX(4), RX(5), RX(6), RX(7), RX(8), RX(9)
...J + K ===> L...
... C + L + V + AB ===> AE

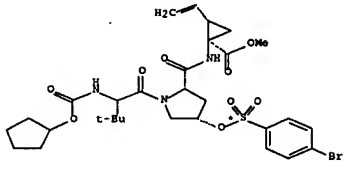


J



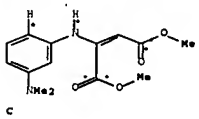
K

7
STEPS



L

START NEXT REACTION SEQUENCE



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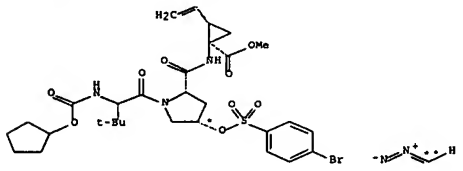
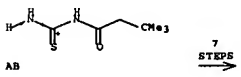


L V



AB

7 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2

SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

RX(9) RCT AC 851009-72-8

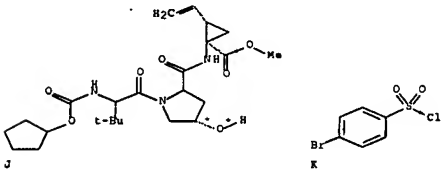
STAGE(1)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, room temperature

STAGE(2)
RGT AF 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 6

STAGE(3)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON 15 minutes, room temperature

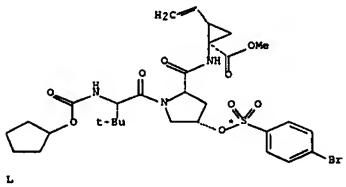
PRO AE 851009-74-0

RX(55) OF 55 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(5), RX(6), RX(7), RX(8), RX(9)
AND REACTION SEQUENCE RX(1), RX(2), RX(4), RX(5), RX(6), RX(7), RX(8), RX(9)
...J + K ===> L...
...A + B + L + V + AB ===> AE



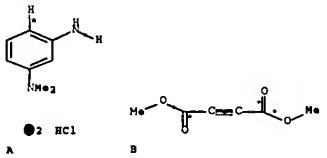
J K

8 STEPS

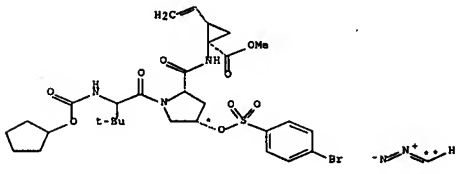


L

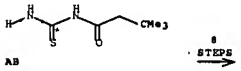
START NEXT REACTION SEQUENCE



A B



L V



AB

8 STEPS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(3) RCT J 572924-77-7, K 98-58-8

STAGE(1)
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT M 121-44-8 Et3N
CON SUBSTAGE(1) 3 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature
SUBSTAGE(4) 18 hours, room temperature

PRO L 801282-34-8

RX(1) RCT A 3575-32-4

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON neutralized

STAGE(2)
RCT B 762-42-5
RGT E 62-53-3 PhNH2
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) heated
SUBSTAGE(3) 2 hours, 65 deg C
SUBSTAGE(4) 14 hours, room temperature

PRO C 791835-61-5
NTE exothermic reaction in second stage, incremental addition of aniline in second stage

RX(2) RCT C 791835-61-5
PRO H 791835-62-6
SOL 101-84-8 PhOPh
CON SUBSTAGE(1) 5 minutes, 250 deg C -> 230 deg C
SUBSTAGE(2) 7 minutes, 230 deg C -> 245 deg C
SUBSTAGE(3) cooled
SUBSTAGE(4) 0 deg C
NTE extended heating at 250 degree celsius would give decarboxylation of desired ester, reaction is done in two batches

RX(4) RCT H 791835-62-6, L 801282-34-8
RGT Q 534-17-8 Cs2CO3
PRO P 851009-68-2
SOL 872-50-4 NMEP
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, 72 deg C

RX(5) RCT P 851009-68-2
RGT T 1310-73-2 NaOH
PRO S 851009-69-3
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1.5 hours, room temperature

RX(6) RCT S 851009-69-3

STAGE(1)
RGT M 121-44-8 Et3N, X 543-27-1 ClCO2Bu-i
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(2)
RCT V 334-88-3
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 minute, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C
SUBSTAGE(3) 45 minutes, room temperature

PRO W 851009-70-6

RX(7) RCT W 851009-70-6

STAGE(1)
RGT AA 10035-10-6 HBr
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 0 deg C
SUBSTAGE(3) 1 hour, 0 deg C

STAGE(2)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO Z 851009-71-7

RX(8) RCT Z 851009-71-7, AB 572923-98-9
PRO AC 851009-72-8
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 5 minutes, heated
SUBSTAGE(2) 1.5 hours
NTE overall yield over 4 steps is 53%

RX(9) RCT AC 851009-72-8

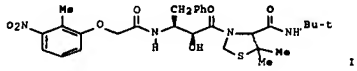
STAGE(1)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 5 hours, room temperature

STAGE(2)
RGT AF 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 6

STAGE(3)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 67-56-1 MeOH, 109-99-9 THF
CON 15 minutes, room temperature

PRO AE 851009-74-0

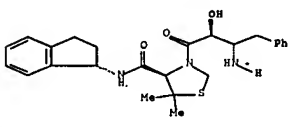
L12 ANSWER 2 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:94101 CASREACT Full-text
TITLE: Design and synthesis of dipeptide-type HIV-1 protease inhibitors with high antiviral activity
AUTHOR(S): Kimura, Tooru; Hidaka, Koushi; Abdel-Rahman, Hamdy M.; Matsumoto, Hikaru; Tanaka, Yoshiaki; Matsui, Yasuko; Hayashi, Yoshio; Kiso, Yoshiaki
CORPORATE SOURCE: Department of Medicinal Chemistry, Center for Frontier Research in Medicinal Science, Kyoto Pharmaceutical University, Kyoto, 607-8412, Japan
SOURCE: Peptide Science (2003), Volume Date 2004, 40th, 241-244
CODEN: PSCIFO; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



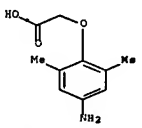
I

AB A symposium report. A series of peptidomimetic HIV protease inhibitors, e.g. I, containing allophenylnorstatine [Apns, (2S,3S)-3-amino-2-hydroxy-4- phenylbutyric acid] with a hydroxymethylcarbonyl (HMC) isostere as a transition-state mimetic was designed and synthesized. From the structure-activity relationship studies, potent dipeptide-type inhibitors having high antiviral activity either in the absence or in the presence of 50% human serum were discovered.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(9) OF 108 ...X + R ===> Y

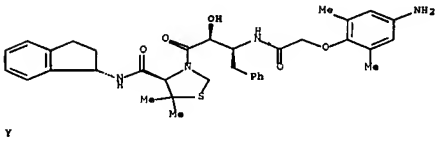


X



R

(9)



Y

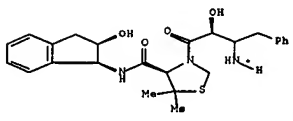
RX(9) RCT X 470697-22-2, R 467446-90-8

STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

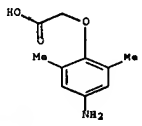
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Y 819083-80-2

RX(10) OF 108 ...Z + R ===> AA

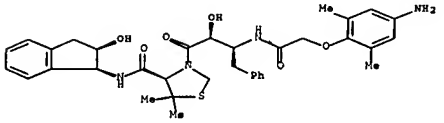


Z



R

(10)



AA

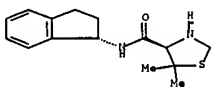
RX(10) RCT Z 819083-90-4, R 467446-90-8

STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

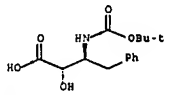
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO AA 819083-81-3

RX(24) OF 108 ...AO + AZ ===> X...

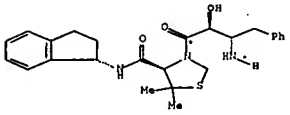


AO



AZ

(24)



X

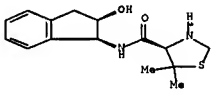
RX(24) RCT AO 819083-85-7, AZ 116661-86-0

STAGE(1)
RGT D 25952-53-8 EDAP

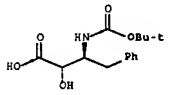
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO X 478697-22-2

RX(25) OF 108 ...AQ + AZ ===> Z...

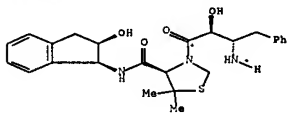


AQ



AZ

(25)



Z

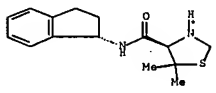
RX(25) RCT AQ 819083-86-8, AZ 116661-86-0

STAGE(1)
RGT D 25952-53-8 EDAP

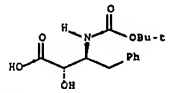
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Z 819083-90-4

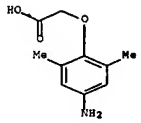
RX(46) OF 108 COMPOSED OF RX(24), RX(9)
RX(46) AO + AZ + R ===> Y



AO

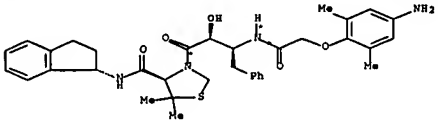


AZ



R

2 STEPS



Y

RX(24) RCT AO 819083-85-7, AZ 116661-86-0

STAGE(1)
RGT D 25952-53-8 EDAP

STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO X 478697-22-2

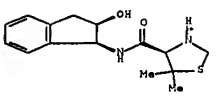
RX(9) RCT X 478697-22-2, R 467446-90-8

STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

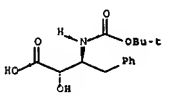
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Y 819083-80-2

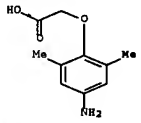
RX(47) OF 108 COMPOSED OF RX(25), RX(10)
RX(47) AQ + AZ + R ===> AA



AQ

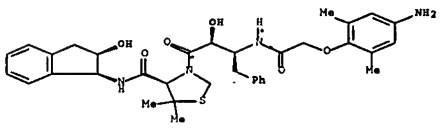


AZ



R

2 STEPS



AA

RX(25) RCT AQ 819083-86-8, AZ 116661-86-0

STAGE(1)
RGT D 25952-53-8 EDAP

STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Z 819083-90-4

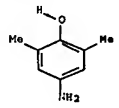
RX(10) RCT Z 819083-90-4, R 467446-90-8

STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

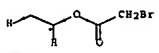
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO AA 819083-81-3

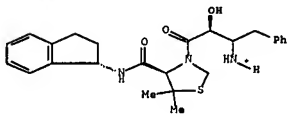
RX(65) OF 108 COMPOSED OF RX(35), RX(9)
RX(65) BI + BB + X ===> Y



BI

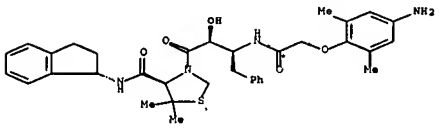


BB



X

2 STEPS



Y

RX(35) RCT BI 15980-22-0, BB 105-36-2

STAGE(1)
RGT BC 584-08-7 K2CO3

STAGE(2)
RGT BD 1310-73-2 NaOH
SOL 7732-18-5 Water

PRO R 467446-90-8

RX(9) RCT X 478697-22-2, R 467446-90-8

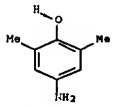
STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

STAGE(2)

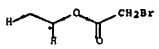
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Y 819083-80-2

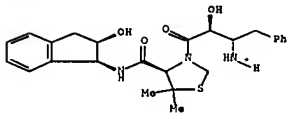
RX(66) OF 108 COMPOSED OF RX(35), RX(10)
RX(66) BI + BB + Z ===> AA



BI

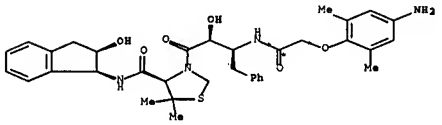


BB



Z

2 STEPS



AA

RX(35) RCT BI 15980-22-0, BB 105-36-2

STAGE(1)
RGT BC 584-08-7 K2CO3

STAGE(2)
RGT BD 1310-73-2 NaOH
SOL 7732-18-5 Water

PRO R 467446-90-8

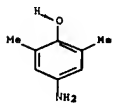
RX(10) RCT Z 819083-90-4, R 467446-90-8

STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

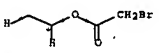
STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO AA 819083-81-3

RX(87) OF 108 COMPOSED OF REACTION SEQUENCE RX(35), RX(9)
AND REACTION SEQUENCE RX(24), RX(9)
...BI + BB ===> R...
... AO + AZ + R ===> Y

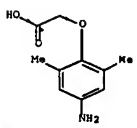


BI



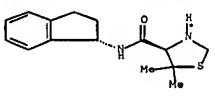
BB

2 STEPS

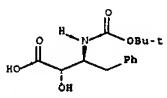


R

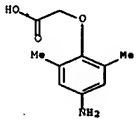
START NEXT REACTION SEQUENCE



AO

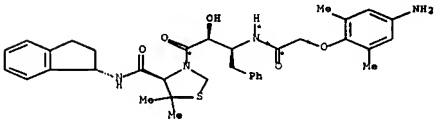


AZ



R

2 STEPS



Y

RX(35) RCT BI 15980-22-0, BB 105-36-2

STAGE(1)
RGT BC 584-08-7 K2CO3

STAGE(2)
RGT BD 1310-73-2 NaOH
SOL 7732-18-5 Water

PRO R 467446-90-8

RX(24) RCT AO 819083-85-7, AZ 116661-86-0

STAGE(1)
RGT D 25952-53-8 EDAP

STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO X 478697-22-2

RX(9) RCT X 478697-22-2, R 467446-90-8

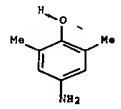
STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

STAGE(2)
RGT O 7647-01-0 HCl

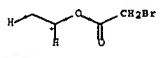
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Y 819083-90-2

RX(89) OF 108 COMPOSED OF REACTION SEQUENCE RX(35), RX(10)
AND REACTION SEQUENCE RX(25), RX(10)
...BI + BB ===> R...
... AQ + AZ + R ===> AA

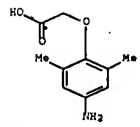


BI



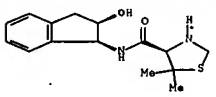
BB

2 STEPS

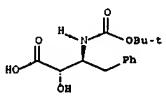


R

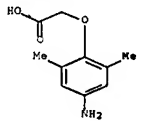
START NEXT REACTION SEQUENCE



AQ

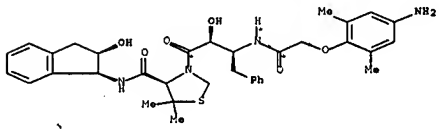


AZ



R

2 STEPS



AA

RX(35) RCT BI 15980-22-0, BB 105-36-2

STAGE(1)
RGT BC 584-08-7 K2CO3

STAGE(2)
RGT BD 1310-73-2 NaOH
SOL 7732-18-5 Water

PRO R 467446-90-8

RX(25) RCT AQ 819083-86-8, AZ 116661-86-0

STAGE(1)
RGT D 25952-53-8 EDAP

STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Z 819083-90-4

RX(10) RCT Z 819083-90-4, R 467446-90-8

STAGE(1)
RGT D 25952-53-8 EDAP, E 2592-95-2 1-Benzotriazolol
SOL 68-12-2 DMF

STAGE(2)
RGT O 7647-01-0 HCl
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO AA 819083-81-3

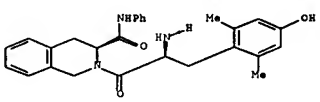
L12 ANSWER 3 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:263738 CASREACT Full-text
TITLE: Synthesis and opioid activity of N,N-dimethyl-Dmt-Tic-NH-CH(R)-R' analogues: acquisition of potent δ antagonism
AUTHOR(S): Salboni, Gianfranco; Salvadori, Severo; Guerrini, Remo; Negri, Lucia; Giannini, Elisa; Bryant, Sharon D.; Jinsmaa, Yunden; Lazarus, Lawrence H.
CORPORATE SOURCE: Department of Toxicology, University of Cagliary, Cagliary, I-09126, Italy
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(24), 5435-5441
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N,N-Dimethylation of the H-Dmt-Tic-NH-CH(R)-R' series of compds. produced no significant effect on the high δ-opioid receptor affinity (Ki=0.035-0.454 nM), but dramatically decreased that for the μ-opioid receptor. The effect of N-methylation was independent of the length of the linker (R); however, the bioactivities were affected by the chemical composition of the third aromatic group (R'): Ph (Ph) (5'-6') elicited a greater reduction in μ-affinity (40-70-fold) compared to analogs containing 1H-benzimidazole-2-yl (Bid) (9-fold). The major consequences of N,N-dimethylation on in vitro bioactivity were: (i) a loss of δ-agonism coupled with the appearance of potent δ antagonism; and (ii) a consistent loss of μ-affinity resulted in enhanced δ-opioid receptor selectivity. With the exception of one compound, the change in the hydrophobic environment at the N-terminus and formation of a tertiary amine by N,N-dimethylation in analogs of the Dmt-Tic pharmacophore produced potent δ-selective antagonists.

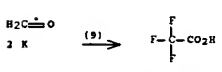
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(9) OF 62 ...Z + 2 K ===> AA

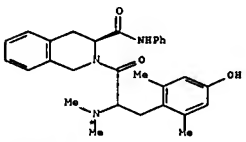
Z: CM 1



Z: CM 2



AA: CM 1
YIELD 89%



AA: CM 2
YIELD 89%

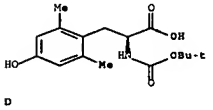
RX(9) RCT Z 673461-36-4, K 50-00-0

STAGE(1)
RGT G 64-19-7 AcOH, M 25895-60-7 NaBH3CN, N 109-02-4 N-Methylmorpholine
SOL 7732-18-5 Water, 75-05-8 MeCN
CON SUBSTAGE(1) 10 minutes, room temperature
SUBSTAGE(2) 15 minutes, room temperature

STAGE(2)
RGT E 76-05-1 F3CCO2H
CON room temperature, acidify

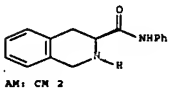
PRO AA 859231-90-6

RX(19) OF 62 ...D + AM ===> AN...



D

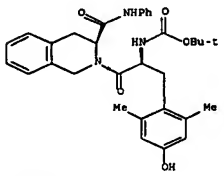
AM: CM 1



AM: CM 2

(19)

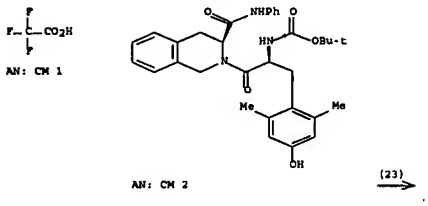
AN: CM 1
YIELD 62%



AN: CM 2
YIELD 82%

RX(19) RCT D 99953-00-1, AM 673461-29-5
RGT H 2592-95-2 1-Benzotriazolol, I 25952-53-8 EDAP
PRO AN 673461-31-9
CON room temperature

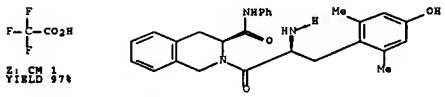
RX(23) OF 62 ...AN ===> Z...



AN: CM 1

AN: CM 2

(23)



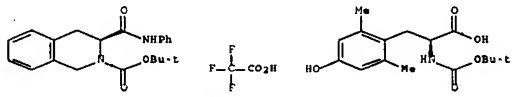
Z: CM 1
YIELD 97%

Z: CM 2
YIELD 97%

RX(23) RCT AN 673461-31-9
RGT E 76-05-1 F3CCO2H

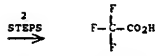
PRO Z 673461-36-4
CON room temperature

RX(34) OF 62 COMPOSED OF RX(18), RX(19)
RX(34) AL + E + D ===> AN

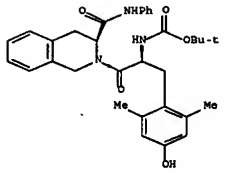


AL E D

2 STEPS



AN: CM 1
YIELD 82%

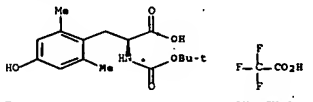


AN: CM 2
YIELD 82%

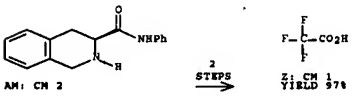
RX(18) RCT AL 673461-28-4, E 76-05-1
PRO AM 673461-29-5
CON room temperature

RX(19) RCT D 99953-00-1, AM 673461-29-5
RGT H 2592-95-2 1-Benzotriazolol, I 25952-53-8 EDAP
PRO AN 673461-31-9
CON room temperature

RX(35) OF 62 COMPOSED OF RX(19), RX(23)
RX(35) D + AM ===> Z



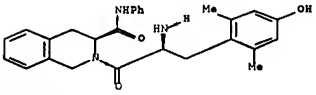
D AM: CM 1



AM: CM 2

2 STEPS

Z: CM 1
YIELD 97%

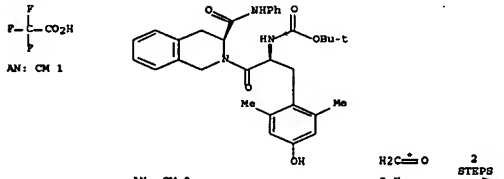


Z: CM 2
YIELD 97%

RX(19) RCT D 99953-00-1, AM 673461-29-5
RGT H 2592-95-2 1-Benzotriazolol, I 25952-53-8 EDAP
PRO AN 673461-31-9
CON room temperature

RX(23) RCT AN 673461-31-9
RGT E 76-05-1 F3CCO2H
PRO Z 673461-36-4
CON room temperature

RX(39) OF 62 COMPOSED OF RX(23), RX(9)
RX(39) AN + 2 K ===> AA

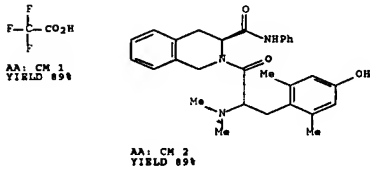


AN: CM 1

AN: CM 2

H2C=O
2 K

2 STEPS



AA: CM 1
YIELD 89%

AA: CM 2
YIELD 89%

RX(23) RCT AN 673461-31-9
RGT E 76-05-1 F3CCO2H
PRO Z 673461-36-4
CON room temperature

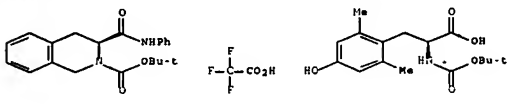
RX(9) RCT Z 673461-36-4, K 50-00-0

STAGE(1)
RGT G 64-19-7 AcOH, M 25895-60-7 NaBH3CN, N 109-02-4 N-Methylmorpholine
SOL 7732-18-5 Water, 75-05-8 MeCN
CON SUBSTAGE(1) 10 minutes, room temperature
SUBSTAGE(2) 15 minutes, room temperature

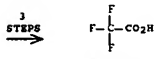
STAGE(2)
RGT E 76-05-1 F3CCO2H
CON room temperature, acidify

PRO AA 859231-90-6

RX(47) OF 62 COMPOSED OF RX(18), RX(19), RX(23)
RX(47) AL + E + D ===> Z

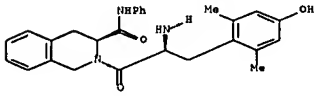


AL E D



3 STEPS

Z; CM 1
YIELD 97%



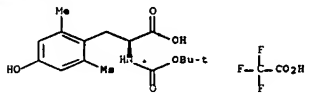
Z; CM 2
YIELD 97%

RX(18) RCT AL 673461-28-4, E 76-05-1
PRO AM 673461-29-5
CON room temperature

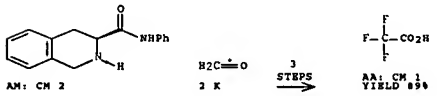
RX(19) RCT D 99953-00-1, AM 673461-29-5
RGT H 2592-95-2 1-Benzotriazolol, I 25952-53-8 EDAP
PRO AN 673461-31-9
CON room temperature

RX(23) RCT AN 673461-31-9
RGT E 76-05-1 F3CCO2H
PRO Z 673461-36-4
CON room temperature

RX(49) OF 62 COMPOSED OF RX(19), RX(23), RX(9)
RX(49) D + AM + 2 K ===> AA



D AM: CM 1



AM: CM 2 2 K 3 STEPS AA; CM 1
YIELD 89%

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(19) RCT D 99953-00-1, AM 673461-29-5
RGT H 2592-95-2 1-Benzotriazolol, I 25952-53-8 EDAP
PRO AN 673461-31-9
CON room temperature

RX(23) RCT AN 673461-31-9
RGT E 76-05-1 F3CCO2H
PRO Z 673461-36-4
CON room temperature

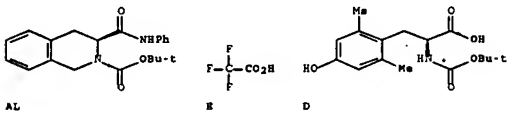
RX(9) RCT Z 673461-36-4, K 50-00-0

STAGE(1)
RGT G 64-19-7 AcOH, M 25895-60-7 NaBH3CN, N 109-02-4 N-Methylmorpholine
SOL 7732-18-5 Water, 75-05-8 MeCN
CON SUBSTAGE(1) 10 minutes, room temperature
SUBSTAGE(2) 15 minutes, room temperature

STAGE(2)
RGT E 76-05-1 F3CCO2H
CON room temperature, acidify

PRO AA 859231-90-6

RX(50) OF 62 COMPOSED OF RX(18), RX(19), RX(23), RX(9)
RX(50) AL + E + D + 2 K ===> AA



AL E D

2 K 4 STEPS

AA; CM 1
YIELD 89%

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(18) RCT AL 673461-28-4, E 76-05-1
PRO AM 673461-29-5
CON room temperature

RX(19) RCT D 99953-00-1, AM 673461-29-5
RGT H 2592-95-2 1-Benzotriazolol, I 25952-53-8 EDAP
PRO AN 673461-31-9
CON room temperature

RX(23) RCT AN 673461-31-9
RGT E 76-05-1 F3CCO2H
PRO Z 673461-36-4
CON room temperature

RX(9) RCT Z 673461-36-4, K 50-00-0

STAGE(1)
RGT G 64-19-7 AcOH, M 25895-60-7 NaBH3CN, N 109-02-4 N-Methylmorpholine
SOL 7732-18-5 Water, 75-05-8 MeCN
CON SUBSTAGE(1) 10 minutes, room temperature
SUBSTAGE(2) 15 minutes, room temperature

STAGE(2)
RGT E 76-05-1 F3CCO2H
CON room temperature, acidify

PRO AA 859231-90-6

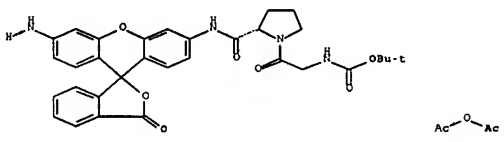
L12 ANSWER 4 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:183296 CASREACT Full-text
TITLE: Transcellular Proteolysis Demonstrated by Novel Cell Surface-associated Substrates of Dipeptidyl Peptidase IV (CD26)
AUTHOR(S): Lorey, Susan; Faust, Juergen; Mrestani-Klaus, Carmen;

Kaehne, Thilo; Ansorge, Siegfried; Neubert, Klaus; Buehling, Frank
CORPORATE SOURCE: Institute of Biochemistry, Department of Biochemistry and Biotechnology, Martin-Luther-University Halle-Wittenberg, Halle (Saale), D-06120, Germany
SOURCE: Journal of Biological Chemistry (2002), 277(36), 33170-33177
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proteolytic enzymes contribute to the regulation of cellular functions such as cell proliferation and death, cytokine production, and matrix remodeling. Dipeptidyl peptidase IV (DP IV) catalyzes the cleavage of several cytokines and thereby contributes to the regulation of cytokine production and the proliferation of immune cells. Here we show for the first time that cell surface-bound DP IV catalyzes the cleavage of specific substrates that are associated with the cellular surface of neighboring cells. Rhodamine 110 (R110), a highly fluorescent xanthene dye, was used to synthesize dipeptidyl peptidase IV (DP IV/CD26) substrates Gly(Ala)-Pro-R110-R, thus facilitating a stable binding of the fluorescent moiety on the cell surface. The fixation resulted from the interaction with the reactive anchor rhodamine and allowed the quantification of cellular DP IV activity on single cells. The reactivity, length, and hydrophobicity of rhodamine was characterized as the decisive factor that facilitated the determination of cellular DP IV activity. Using fluorescence microscopy, it was possible to differentiate between different DP IV activities. The hydrolysis of cell-bound substrates Xaa-Pro-R110-R by DP IV of neighboring cells and by soluble DP IV was shown using flow cytometry. These data demonstrate that ectopeptidases such as DP IV may be involved in communication between blood cells via proteolysis of cell-associated substrates.

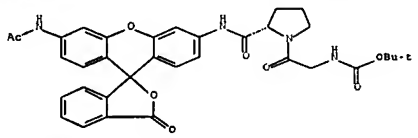
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(3) OF 50 ...C + I ===> J...



C I

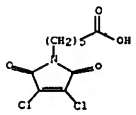
(3)



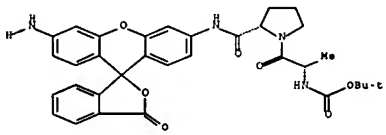
J
YIELD 96%

RX(3) RCT C 498539-64-3, I 108-24-7
PRO J 586962-97-2
SOL 110-86-1 Pyridine
CON 24 hours, room temperature

RX(10) OF 50 ...W + H ===> Y...

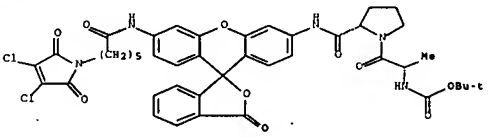


W



H

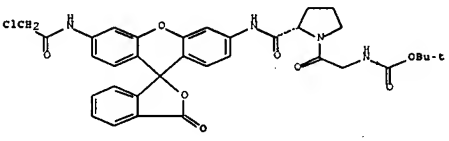
(10)



Y
YIELD 35%

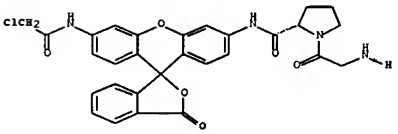
RX(10) RCT W 101310-84-3, H 498539-65-4
ROT E 25952-53-8 EDAP
PRO Y 586961-92-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 20 hours, room temperature
SUBSTAGE(3) 6 hours, room temperature

RX(13) OF 50 ...M ===> AD



M

(13)

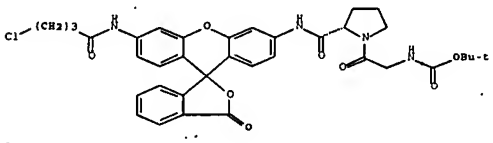


AD

RX(13) RCT M 586961-19-6
RGT AE 76-05-1 F3CCO2H
PRO AD 498539-66-5

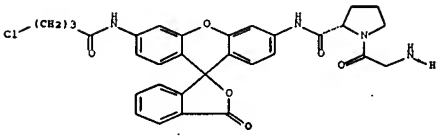
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(14) OF 50 ...O ===> AG



O

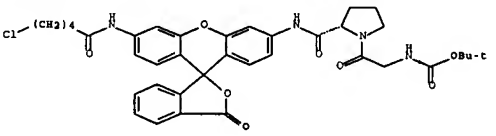
(14)



AG

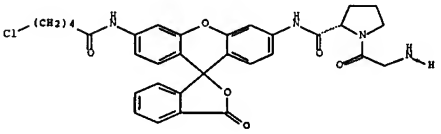
RX(14) RCT O 586961-24-2
RGT AE 76-05-1 F3CCO2H
PRO AG 498539-67-6
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(15) OF 50 AH ===> AI



AH

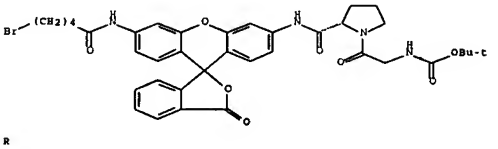
(15)



AI

RX(15) RCT AH 586961-51-5
RGT AE 76-05-1 F3CCO2H
PRO AI 498539-68-7
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(16) OF 50 ...R ===> AJ



R

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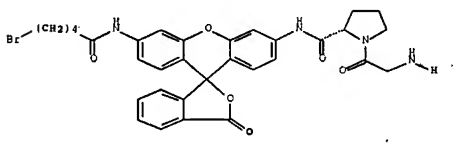
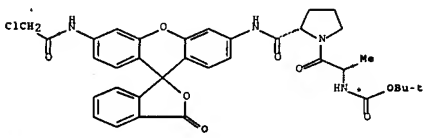


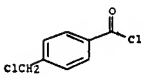
AJ

RX(16) RCT R 586961-54-8
RGT AE 76-05-1 F3CCO2H
PRO AJ 498539-69-8
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(17) OF 50 AK + S ===> T



AK



S

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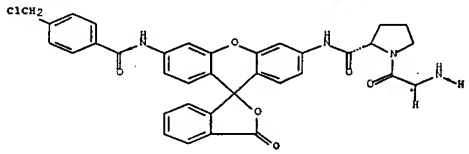
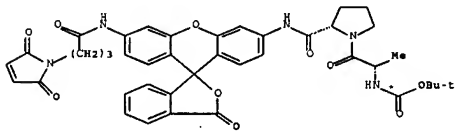


T

RX(17) RCT AK 586961-74-2, S 876-08-4
RGT AE 76-05-1 F3CCO2H
PRO T 498539-70-1
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(18) OF 50 ...AA ===> AL



AA

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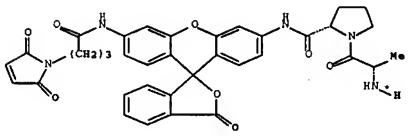
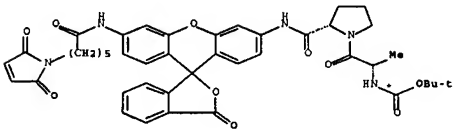


AL

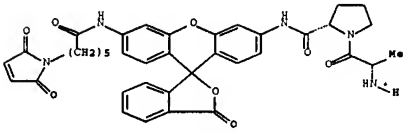
RX(18) RCT AA 586961-80-0
RGT AE 76-05-1 F3CCO2H
PRO AL 498539-71-2
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(19) OF 50 ...AC ===> AM



AC

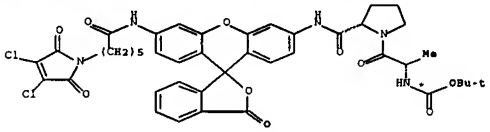
(19)



AM

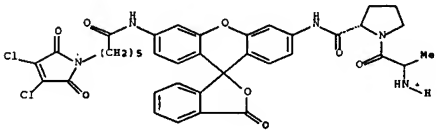
RX(19) RCT AC 586961-89-9
RGT AE 76-05-1 F3CCO2H
PRO AM 498539-72-3
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(20) OF 50 ...Y ===> AN



Y

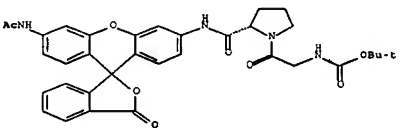
(20)



AN

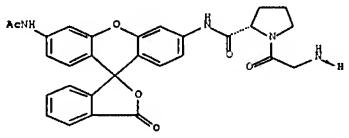
RX(20) RCT Y 586961-92-4
RGT AO 7647-01-0 HCl, AP 64-19-7 AcOH
PRO AN 498539-73-4
CON 30 minutes, room temperature

RX(21) OF 50 ...J ===> AQ



J

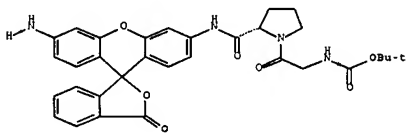
(21)



AQ

RX(21) RCT J 586962-97-2
RGT AO 7647-01-0 HCl, AP 64-19-7 AcOH
PRO AQ 498539-74-5
CON 30 minutes, room temperature

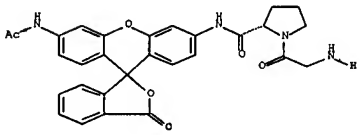
RX(31) OF 50 COMPOSED OF RX(3), RX(21)
RX(31) C + I ===> AQ



C

I

2 STEPS

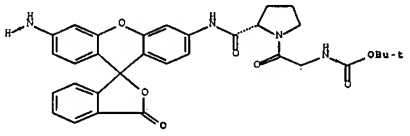


AQ

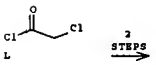
RX(3) RCT C 498539-64-3, I 108-24-7
PRO J 586962-97-2
SOL 110-86-1 Pyridine
CON 24 hours, room temperature

RX(21) RCT J 586962-97-2
RGT AO 7647-01-0 HCl, AP 64-19-7 AcOH
PRO AQ 498539-74-5
CON 30 minutes, room temperature

RX(32) OF 50 COMPOSED OF RX(4), RX(13)
RX(32) C + L ===> AD

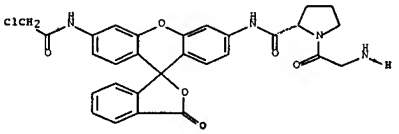


C



L

2 STEPS



AD

RX(4) RCT C 498539-64-3

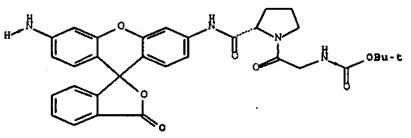
STAGE(1)
SOL 68-12-2 DMF
CON room temperature -> 4 deg C

STAGE(2)
RCT L 79-04-9
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 1 hour, room temperature

PRO M 586961-19-5

RX(13) RCT M 586961-19-5
RGT AE 76-05-1 F3CCO2H
PRO AD 498539-66-5
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(33) OF 50 COMPOSED OF RX(5), RX(14)
RX(33) C + N ===> AG



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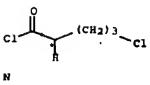

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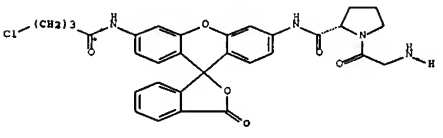
2 STEPS



AG

RX(5) RCT C 498539-64-3

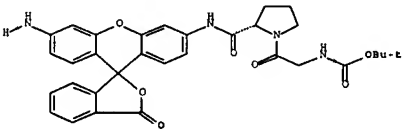
STAGE(1)
SOL 68-12-2 DMF
CON room temperature -> 4 deg C

STAGE(2)
RCT N 1575-61-7
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 1 hour, room temperature

PRO O 586961-24-2

RX(14) RCT O 586961-24-2
RGT AE 76-05-1 F3CCO2H
PRO AG 498539-67-6
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(34) OF 50 COMPOSED OF RX(6), RX(14)
RX(34) C + P ===> AG



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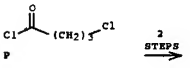

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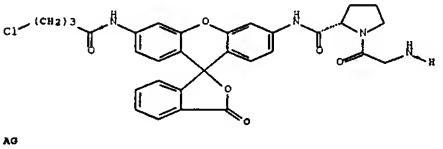
2 STEPS



AG

RX(6) RCT C 498539-64-3

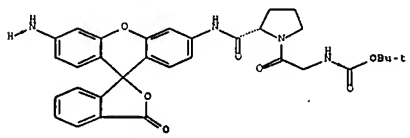
STAGE(1)
SOL 68-12-2 DMF
CON room temperature -> 4 deg C

STAGE(2)
RCT P 4635-59-0
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 1 hour, room temperature

PRO O 586961-24-2

RX(14) RCT O 586961-24-2
RGT AE 76-05-1 F3CCO2H
PRO AG 498539-67-6
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(35) OF 50 COMPOSED OF RX(7), RX(16)
RX(35) C + Q ===> AJ



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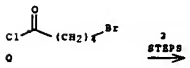
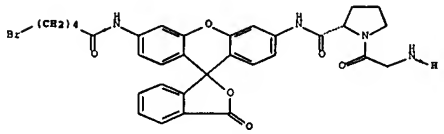


Q

2 STEPS



AJ

RX(7) RCT C 498539-64-3

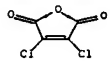
STAGE(1)
SOL 68-12-2 DMF
CON room temperature -> 4 deg C

STAGE(2)
RCT Q 4509-90-4
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 1 hour, room temperature

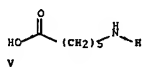
PRO R 586961-54-8

RX(16) RCT R 586961-54-8
RGT AE 76-05-1 F3CCO2H
PRO AJ 498539-69-8
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(36) OF 50 COMPOSED OF RX(9), RX(10)
RX(36) U + V + H ===> Y



U



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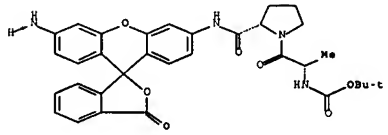
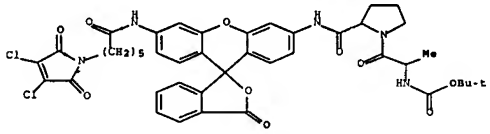


H

2 STEPS

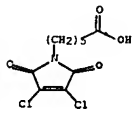


Y
YIELD 35%

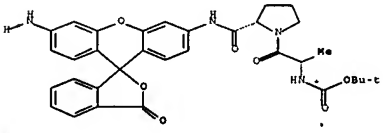
RX(9) RCT U 1122-17-4, V 60-32-2
PRO W 101310-84-3
SOL 109-99-9 THF
CON 3 hours, reflux

RX(10) RCT W 101310-84-3, H 498539-65-4
RGT E 25952-53-8 EDAP
PRO Y 586961-92-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 20 hours, room temperature
SUBSTAGE(3) 6 hours, room temperature

RX(37) OF 50 COMPOSED OF RX(10), RX(20)
RX(37) W + H ===> AN

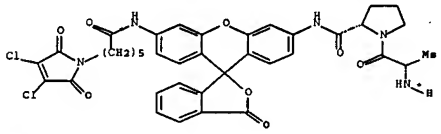


W



H

2 STEPS

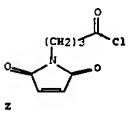


AN

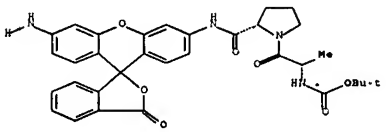
RX(10) RCT W 101310-84-3, H 498539-65-4
RGT E 25952-53-8 EDAP
PRO Y 586961-92-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 20 hours, room temperature
SUBSTAGE(3) 6 hours, room temperature

RX(20) RCT Y 586961-92-4
RGT AO 7647-01-0 HCl, AP 64-19-7 AcOH
PRO AN 498539-73-4
CON 30 minutes, room temperature

RX(38) OF 50 COMPOSED OF RX(11), RX(18)
RX(38) Z + H ===> AL

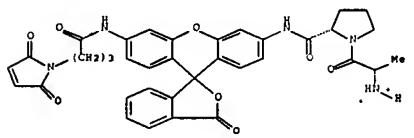


Z



H

2 STEPS



AL

RX(11) RCT Z 116965-29-8

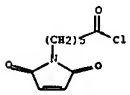
STAGE(1)
SOL 68-12-2 DMF
CON room temperature -> 4 deg C

STAGE(2)
RCT H 498539-65-4
RGT D 100-74-3 4-Ethylmorpholine, E 25952-53-8 EDAP
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 6 hours, room temperature

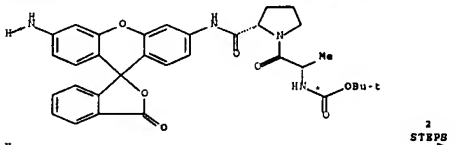
PRO AA 586961-80-0

RX(18) RCT AA 586961-80-0
RGT AE 76-05-1 F3CCO2H
PRO AL 498539-71-2
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(39) OF 50 COMPOSED OF RX(12), RX(19)
RX(39) AB + H ===> AM

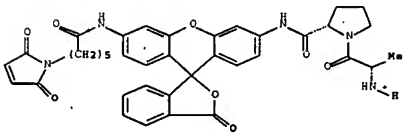


AB



H

2 STEPS



AM

RX(12) RCT AB 82333-93-5

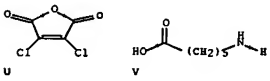
STAGE(1)
SOL 68-12-2 DMF
CON room temperature -> 4 deg C

STAGE(2)
RCT H 498539-65-4
RGT D 100-74-3 4-Ethylmorpholine, E 25952-53-8 EDAP
CON SUBSTAGE(1) 1 hour, 4 deg C
SUBSTAGE(2) 6 hours, room temperature

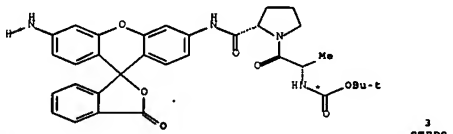
PRO AC 586961-89-9

RX(19) RCT AC 586961-89-9
RGT AE 76-05-1 F3CCO2H
PRO AM 498539-72-3
SOL 75-09-2 CH2Cl2
CON 3 hours, room temperature

RX(49) OF 50 COMPOSED OF RX(9), RX(10), RX(20)
RX(49) U + V + H ===> AN

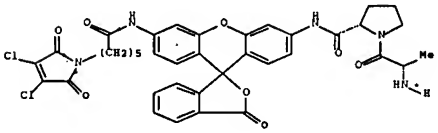


U V



H

3 STEPS



AN

RX(9) RCT U 1122-17-4, V 60-32-2
PRO W 101310-84-3
SOL 109-99-9 THF
CON 3 hours, reflux

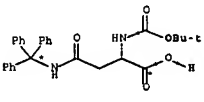
RX(10) RCT W 101310-84-3, H 498539-65-4
RGT E 25952-53-8 EDAP
PRO Y 586961-92-4
SOL 68-12-2 DMF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 20 hours, room temperature
SUBSTAGE(3) 6 hours, room temperature

RX(20) RCT Y 586961-92-4
RGT AO 7647-01-0 HCl, AP 64-19-7 AcOH
PRO AN 498539-73-4
CON 30 minutes, room temperature

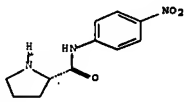
L12 ANSWER 5 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:247867 CASREACT Full-text
TITLE: Polymer-assisted solution-phase parallel synthesis of dipeptide p-nitroanilides and dipeptide diphenyl phosphonates
AUTHOR(S): Senten, Kristel; Van der Veken, Pieter; Bal, Gunther; Haemers, Achiel; Augustyns, Koen
CORPORATE SOURCE: Department of Medicinal Chemistry, University of

Antwerp (UIA), Antwerp, B-2610, Belg.
SOURCE: Tetrahedron Letters (2001), 42(52), 9135-9138
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This letter describes the parallel synthesis of dipeptide p-nitroanilides and dipeptide di-Ph phosphonates, compds. that can be used as substrates and irreversible inhibitors for the rapid profiling of dipeptidyl peptidases. A polymer-assisted solution-phase synthesis was used for a rapid and clean coupling between easily available building blocks.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 35 A + B ===> C

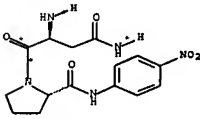


A



B

(1)



C
YIELD 98%

RX(1) RCT A 132388-68-2

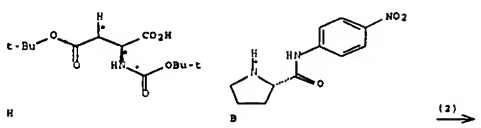
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

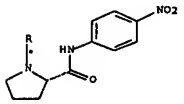
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

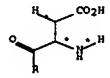
PRO C 90145-75-8
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

RX(2) OF 35 H + B ===> I



H B (2) →





I
YIELD 87%

RX(2) RCT H 1676-90-0

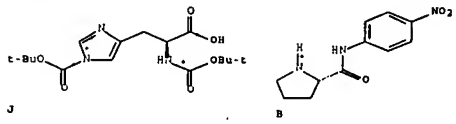
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

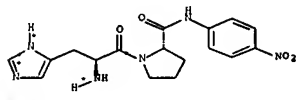
PRO I 60189-48-2
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

RX(3) OF 35 J + B ===> K



J B

(3) →



K
YIELD 42%

RX(3) RCT J 20866-46-0

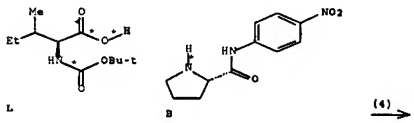
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

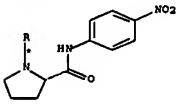
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

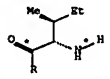
PRO K 99264-68-3
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

RX(4) OF 35 L + B ===> M



L B (4) →





M
YIELD 10%

RX(4) RCT L 13139-16-7

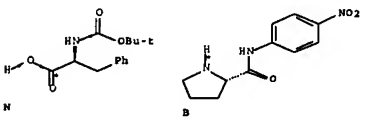
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

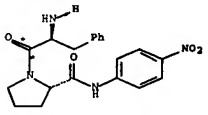
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO M 90145-77-0
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

RX(5) OF 35 N + B ===> O



N B (5) →



O
YIELD 16%

RX(5) RCT N 13734-34-4

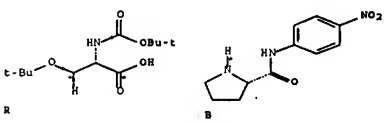
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

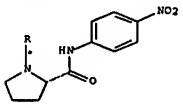
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

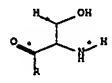
PRO O 90145-72-5
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

RX(7) OF 35 R + B ===> S



R B (7) →





S
YIELD 84%

RX(7) RCT R 13734-38-8

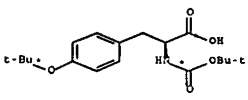
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

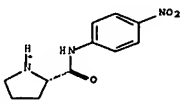
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO S 90145-70-3
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

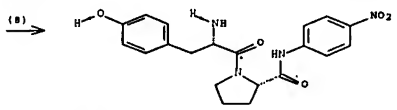
RX(8) OF 35 T + B ===> U



T



B



U
YIELD 18%

RX(8) RCT T 47375-34-8

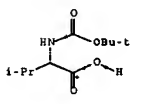
STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

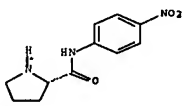
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO U 90145-69-0
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

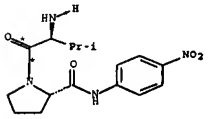
RX(9) OF 35 V + B ===> W



V



B



W
YIELD 30%

RX(9) RCT V 13734-41-3

STAGE(1)
RGT D 2592-95-2 1-Benzotriazolol, E 538-75-0 DCC
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT B 7369-91-7
SOL 75-09-2 CH2Cl2

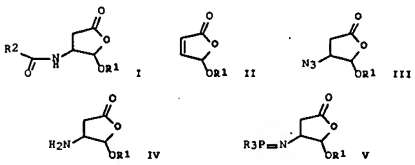
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO W 90145-74-7
NTE polymer-assisted solution-phase synthesis, solid-supported reagent, methylpolystyrene resin used

L12 ANSWER 6 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:344726 CASREACT Full-text
TITLE: Process for preparation of substituted aspartic acid acetals from butenolactones.
INVENTOR(S): Wannamaker, Marion W.; Forster, Cornelia
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

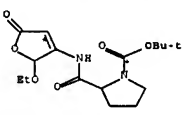
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081330	A2	20011101	WO 2001-US12769	20010419
WO 2001081330	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402128	A1	20011101	CA 2001-2402128	20010419
EP 1278737	A2	20030129	EP 2001-927217	20010419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 2002006658	A	20040428	ZA 2002-6658	20020820
BG 107028	A	20030630	BG 2002-107028	20020822
NO 2002004111	A	20020828	NO 2002-4111	20020828
US 2003119899	A1	20030626	US 2002-229981	20020828
US 7109357	B2	20060919		
BR 2002004426	A	20040608	BR 2002-204426	20021029
PRIORITY APPLN. INFO.:			US 2000-199329P	20000424
			WO 2001-US12769	20010419

OTHER SOURCE(S): MARPAT 135:344726
GI

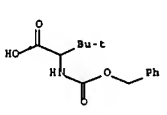


AB Title compds. [I; R1 = (substituted) aliphatyl, aralkyl, heterocyclylalkyl, aryl; R2 = organic radical, preferably a P2-P4 moiety of a caspase inhibitor], were prepared by treatment of butenolactones (II; R1 as above) with N3Y (Y = H, silyl, counterion) to give azidolactones (III; R1 as above) followed by conversion of III to aminolactones (IV) or iminophosphoranes (V; R undefined) and coupling of either with R2CO2H (R2 as above) or a reactive equivalent thereof. Thus, Me3SiN3, HOAc, DBU, and 5-ethoxy-5H-furan-2-one were stirred 24 h in CH2Cl2 to give 73% 4-azido-5-ethoxydihydrofuran-2-one. The latter with (S)-pyrrolidine-1,2- dicarboxylic acid 1-tert-Bu ester was hydrogenated in EtOAc over Pd/C under 1 atm H2 for 1 h; the mixture was diluted with CH2Cl2, filtered, and evaporated The crude mixture was stirred with diisopropylethylamine, EDC, and HOBT in CH2Cl2 for 24 h to give 56% (R)-2-(2-ethoxy-5-oxo-tetrahydrofuran- 3-ylcarbamoyl)pyrrolidine-1-carboxylic acid tert-Bu ester.

RX(11) OF 28 ...AH + AN ===> AK...

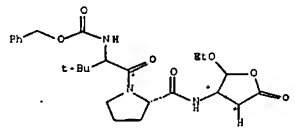


AH



AN

(11)



AK
YIELD 59%

RX(11) RCT AH 370877-09-1

STAGE(1)
RGT AO 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AP 27607-77-8 Me3SiSO3CF3

STAGE(3)
RGT AQ 144-55-8 NaHCO3

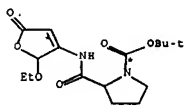
STAGE(4)
SOL 75-09-2 CH2Cl2

STAGE(5)
RCT AN 68222-59-3
RGT W 25952-53-8 EDAP, X 2592-95-2 1-Benzotriazolol
SOL 75-09-2 CH2Cl2

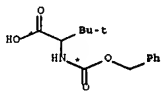
STAGE(6)
SOL 141-78-6 AcOEt

PRO AK 371126-01-1

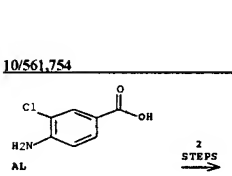
RX(20) OF 28 COMPOSED OF RX(11), RX(10)
RX(20) AH + AN + AL ===> AM



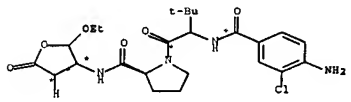
AH



AN



AL



AM
YIELD 62%

RX(11) RCT AH 370877-09-1

STAGE(1)
RGT AO 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AP 27607-77-8 Me3SiSO3CF3

STAGE(3)
RGT AQ 144-55-8 NaHCO3

STAGE(4)
SOL 75-09-2 CH2Cl2

STAGE(5)
RCT AN 68222-59-3
RGT W 25952-53-8 EDAP, X 2592-95-2 1-Benzotriazolol
SOL 75-09-2 CH2Cl2

STAGE(6)
SOL 141-78-6 AcOEt

PRO AK 371126-01-1

RX(10) RCT AK 371126-01-1

STAGE(1)
RGT K 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 141-78-6 AcOEt

STAGE(2)
SOL 75-09-2 CH2Cl2

STAGE(3)

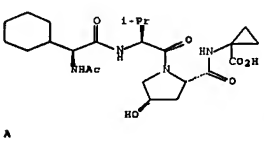
RCT AL 2486-71-7
RGT O 7087-68-5 EtN(Pr-i)2, W 25952-53-8 EDAP

STAGE(4)
SOL 141-78-6 AcOEt

PRO AM 371126-03-3

L12 ANSWER 7 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:195782 CASREACT Full-text
TITLE: Solid-Phase Synthesis of Peptidomimetic Inhibitors for the Hepatitis C Virus NS3 Protease
AUTHOR(S): Poupart, Marc-Andre; Cameron, Dale R.; Chabot, Catherine; Ghiro, Elise; Goudreau, Nathalie; Goulet, Sylvie; Poirier, Martin; Tsantrizos, Youla S.
CORPORATE SOURCE: Department of Chemistry, Boehringer Ingelheim (Canada) Ltd., QC, H7S 2G5, Can.
SOURCE: Journal of Organic Chemistry (2001), 66(14), 4743-4751
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The NS3 serine protease enzyme of the hepatitis C virus (HCV) is essential for viral replication. Short peptides mimicking the N-terminal substrate cleavage products of the NS3 protease are known to act as weak inhibitors of the enzyme and have been used as templates for the design of peptidomimetic inhibitors. Automated solid-phase synthesis of a small library of compds. based on such a peptidomimetic scaffold has led to the identification of potent and highly selective inhibitors of the NS3 protease enzyme.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

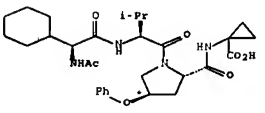
RX(1) OF 32 A + B ===> C



A

B

(1)



C
YIELD 45%

RX(1) RCT A 357292-85-4

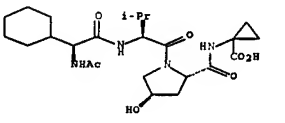
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT B 108-95-2
SOL 109-99-9 THF

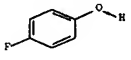
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO C 357292-89-8
NTE stereoselective, solid-supported reactant, Wang resin used

RX(2) OF 32 A + I ===> J

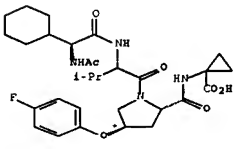


A



I

(2)



J
YIELD 50%

RX(2) RCT A 357292-85-4

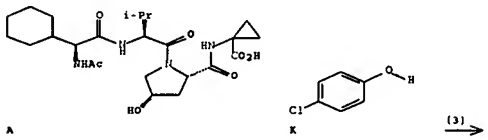
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT I 371-41-5
SOL 109-99-9 THF

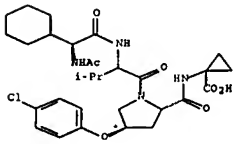
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO J 357292-90-1
NTE stereoselective, solid-supported reactant, Wang resin used

RX(3) OF 32 A + K ===> L



A K



L
YIELD 45%

RX(3) RCT A 357292-85-4

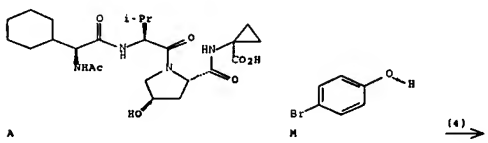
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT K 106-48-9
SOL 109-99-9 THF

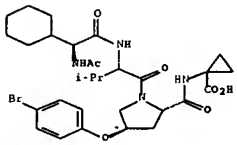
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO L 357292-91-2
NTE stereoselective, solid-supported reactant, Wang resin used

RX(4) OF 32 A + M ===> N



A M



N
YIELD 67%

RX(4) RCT A 357292-85-4

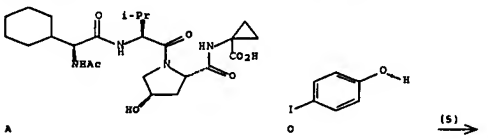
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT M 106-41-2
SOL 109-99-9 THF

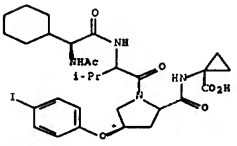
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO N 357292-86-5
NTE stereoselective, solid-supported reactant, Wang resin used

RX(5) OF 32 A + O ===> P



A O



P
YIELD 74%

RX(5) RCT A 357292-85-4

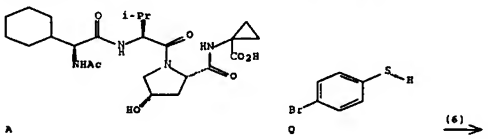
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT O 540-38-5
SOL 109-99-9 THF

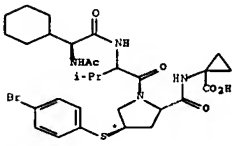
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO P 357292-92-3
NTE stereoselective, solid-supported reactant, Wang resin used

RX(6) OF 32 A + Q ===> R



A Q



R
YIELD 67%

RX(6) RCT A 357292-85-4

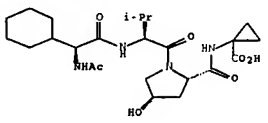
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT Q 106-53-6
SOL 109-99-9 THF

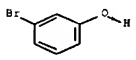
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO R 357292-93-4
NTE stereoselective, solid-supported reactant, Wang resin used

RX(7) OF 32 A + S ===> T

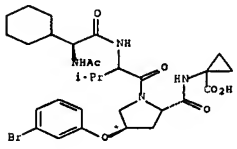


A



S

(7)



T
YIELD 53%

RX(7) RCT A 357292-85-4

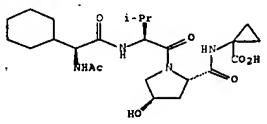
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT S 591-20-8
SOL 109-99-9 THF

STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO T 357292-87-6
NTE stereoselective, solid-supported reactant, Wang resin used

RX(8) OF 32 A + U ===> V



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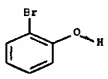
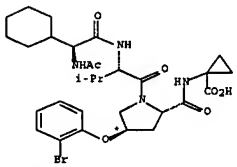


U

(8)



V
YIELD 82%

RX(8) RCT A 357292-85-4

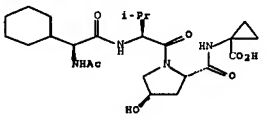
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT U 95-56-7
SOL 109-99-9 THF

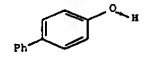
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO V 357292-88-7
NTE stereoselective, solid-supported reactant, Wang resin used

RX(9) OF 32 A + W ===> X

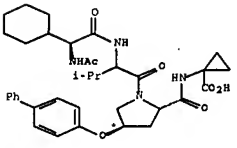


A



W

(9)



X
YIELD 30%

RX(9) RCT A 357292-85-4

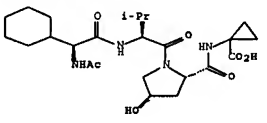
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT W 92-69-3
SOL 109-99-9 THF

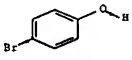
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO X 357292-94-5
NTE stereoselective, solid-supported reactant, Wang resin used

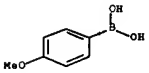
RX(10) OF 32 A + M + Y ===> Z



A

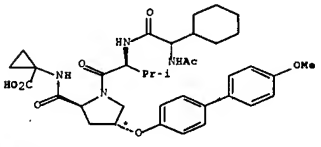


M



Y

(10)



Z
YIELD 23%

RX(10) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT M 106-41-2
SOL 109-99-9 THF

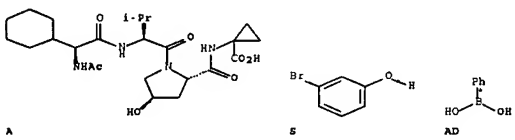
STAGE(3)
RCT Y 5720-07-0
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

STAGE(4)
RGT F 76-05-1 F3CCO2H

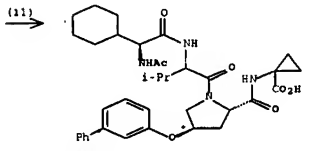
SOL 75-09-2 CH2Cl2

PRO Z 357292-95-6
NTE stereoselective, solid-supported reactant, Wang resin used

RX(11) OF 32 A + S + AD ===> AE



A S AD



AE
YIELD 23%

RX(11) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

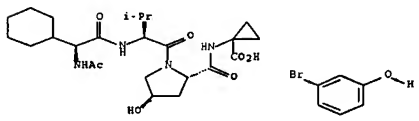
STAGE(2)
RCT S 591-20-8
SOL 109-99-9 THF

STAGE(3)
RCT AD 98-80-6
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

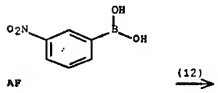
STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AE 357292-96-7
NTE stereoselective, solid-supported reactant, Wang resin used

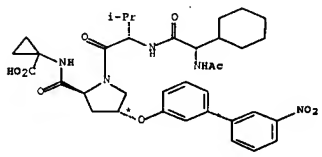
RX(12) OF 32 A + S + AF ===> AG



A S



AF



AG
YIELD 58%

RX(12) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT S 591-20-8
SOL 109-99-9 THF

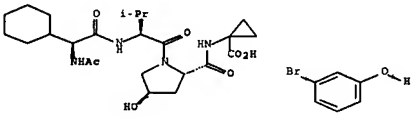
STAGE(3)
RCT AF 13331-27-6
RGT AA 497-19-8 Na2CO3

CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

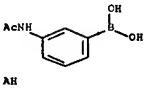
STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AG 357292-97-8
NTE stereoselective, solid-supported reactant, Wang resin used

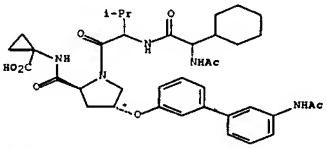
RX(13) OF 32 A + S + AH ===> AI



A S



AH



AI
YIELD 70%

RX(13) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

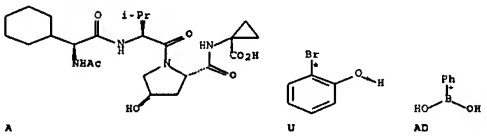
STAGE(2)
RCT S 591-20-8
SOL 109-99-9 THF

STAGE(3)
RCT AH 78887-39-5
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

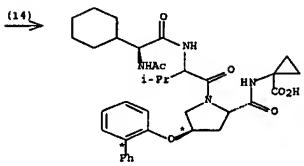
STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AI 357292-98-9
NTE stereoselective, solid-supported reactant, Wang resin used

RX(14) OF 32 A + U + AD ===> AJ



A U AD



AJ
YIELD 44%

RX(14) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT U 95-56-7

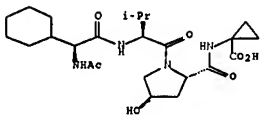
SOL 109-99-9 THF

STAGE(3)
RCT AD 98-80-6
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

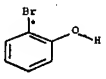
STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AJ 357292-99-0
NTE stereoselective, solid-supported reactant, Wang resin used

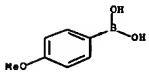
RX(15) OF 32 A + U + Y ===> AK



A



U



Y

(15)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

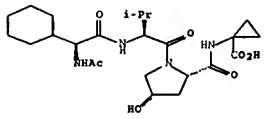
STAGE(2)
RCT U 95-56-7
SOL 109-99-9 THF

STAGE(3)
RCT Y 5720-07-0
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

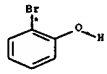
STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AK 357293-00-6
NTE stereoselective, solid-supported reactant, Wang resin used

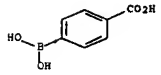
RX(16) OF 32 A + U + AL ===> AM



A



U



AL

(16)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(16) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

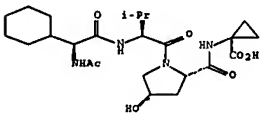
STAGE(2)
RCT U 95-56-7
SOL 109-99-9 THF

STAGE(3)
RCT AL 14047-29-1
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AM 357293-01-7
NTE stereoselective, solid-supported reactant, Wang resin used

RX(17) OF 32 A + AN + AO ===> AP



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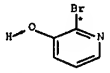

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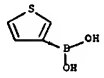
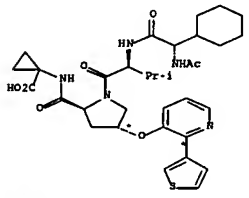


AO

(17)



AP
YIELD 40%

RX(17) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

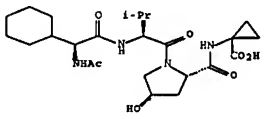
STAGE(2)
RCT AN 6602-32-0
SOL 109-99-9 THF

STAGE(3)
RCT AO 6165-69-1
RGT AA 497-19-8 Na2CO3
CAT 14221-01-3 Pd(PPh3)4
SOL 110-71-4 (CH2OMe)2

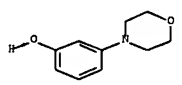
STAGE(4)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AP 357293-02-8
NTE stereoselective, solid-supported reactant, Wang resin used

RX(18) OF 32 A + AQ ===> AR

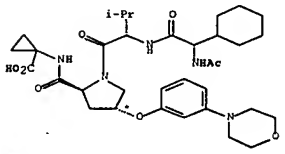


A



AQ

(18)



AR
YIELD 23%

RX(18) RCT A 357292-85-4

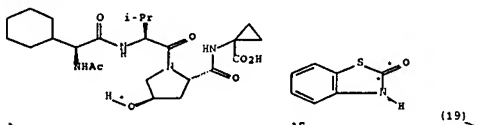
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT AQ 27292-49-5
SOL 109-99-9 THF

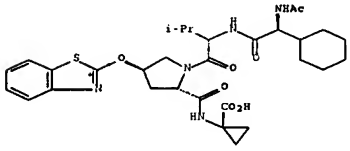
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AR 357293-03-9
NTE stereoselective, solid-supported reactant, Wang resin used

RX(19) OF 32 A + AS ===> AT



A AS (19)



AT
YIELD 60%

RX(19) RCT A 357292-85-4

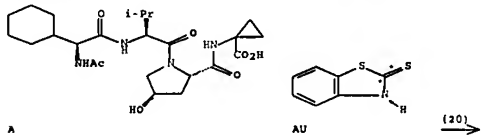
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT AS 934-34-9
SOL 109-99-9 THF

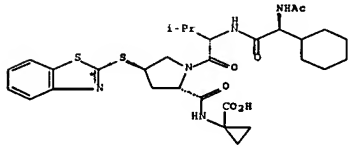
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AT 357293-04-0
NTE stereoselective, solid-supported reactant, Wang resin used

RX(20) OF 32 A + AU ===> AV



A AU (20)



AV
YIELD 77%

RX(20) RCT A 357292-85-4

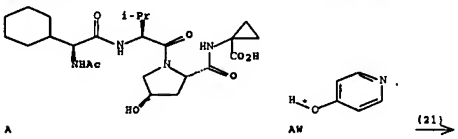
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT AU 149-30-4
SOL 109-99-9 THF

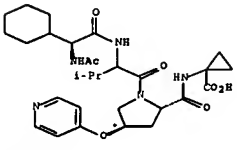
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AV 357293-05-1
NTE stereoselective, solid-supported reactant, Wang resin used

RX(21) OF 32 A + AW ===> AX



A AW (21)



AX
YIELD 26%

RX(21) RCT A 357292-85-4

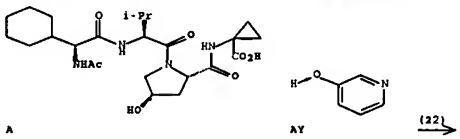
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT AW 626-64-2
SOL 109-99-9 THF

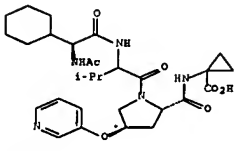
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AX 357293-06-2
NTE stereoselective, solid-supported reactant, Wang resin used

RX(22) OF 32 A + AY ===> AZ



A AY (22)



AZ
YIELD 16%

RX(22) RCT A 357292-85-4

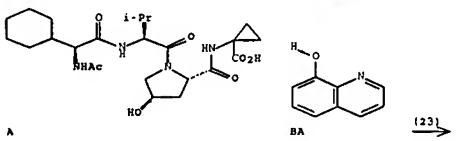
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT AY 109-00-2
SOL 109-99-9 THF

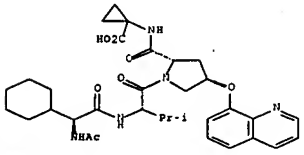
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO AZ 357293-07-3
NTE stereoselective, solid-supported reactant, Wang resin used

RX(23) OF 32 A + BA ===> BB



A BA (23)



BB
YIELD 21%

RX(23) RCT A 357292-85-4

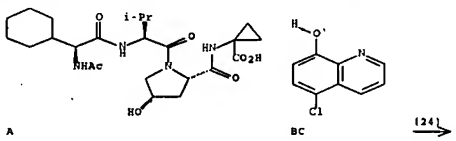
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BA 148-24-3
SOL 109-99-9 THF

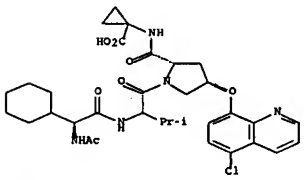
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BB 357293-08-4
NTE stereoselective, solid-supported reactant, Wang resin used

RX(24) OF 32 A + BC ===> BD



A BC (24)



BD
YIELD 50%

RX(24) RCT A 357292-85-4

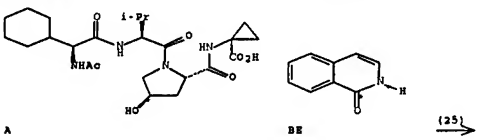
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BC 130-16-5
SOL 109-99-9 THF

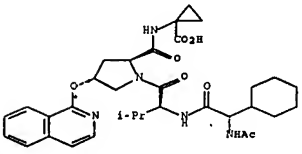
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BD 357293-09-5
NTE stereoselective, solid-supported reactant, Wang resin used

RX(25) OF 32 A + BE ===> BF



A BE (25)



BF
YIELD 41%

RX(25) RCT A 357292-85-4

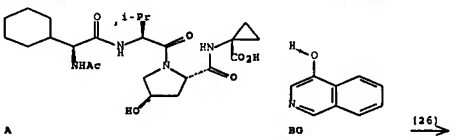
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BE 491-30-5
SOL 109-99-9 THF

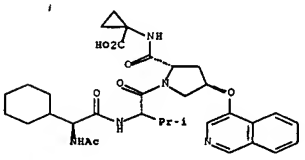
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BF 357293-10-8
NTE stereoselective, solid-supported reactant, Wang resin used

RX(26) OF 32 A + BG ===> BH



A BG (26)



BH
YIELD 23%

RX(26) RCT A 357292-85-4

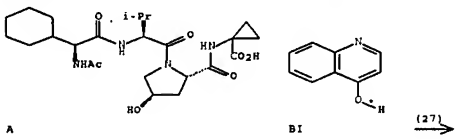
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BG 3336-49-0
SOL 109-99-9 THF

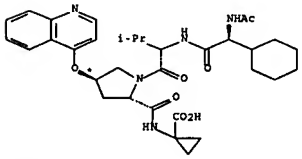
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BH 357293-11-9
NTE stereoselective, solid-supported reactant, Wang resin used

RX(27) OF 32 A + BI ===> BJ



A BI (27)



BJ
YIELD 75%

RX(27) RCT A 357292-85-4

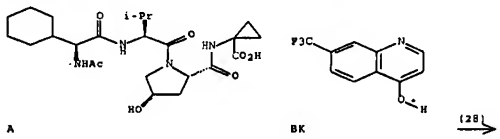
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BI 611-36-9
SOL 109-99-9 THF

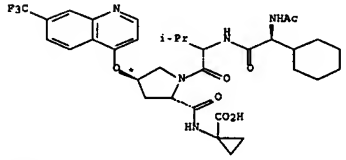
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BJ 357293-12-0
NTE stereoselective, solid-supported reactant, Wang resin used

RX(28) OF 32 A + BK ===> BL



A BK (28)



BL
YIELD 57%

RX(28) RCT A 357292-85-4

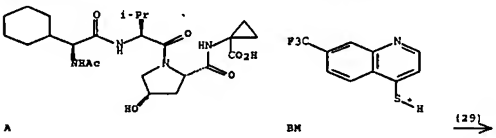
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BK 322-97-4
SOL 109-99-9 THF

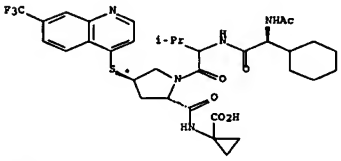
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BL 357293-13-1
NTE stereoselective, solid-supported reactant, Wang resin used

RX(29) OF 32 A + BM ===> BN



A BM (29)



BN
YIELD 61%

RX(29) RCT A 357292-85-4

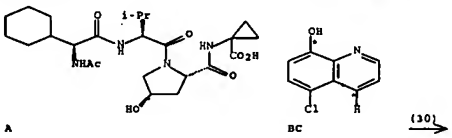
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BM 64415-07-2
SOL 109-99-9 THF

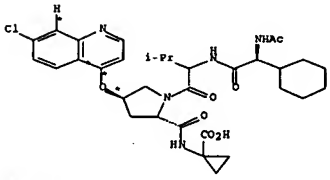
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BN 357293-14-2
NTE stereoselective, solid-supported reactant, Wang resin used

RX(30) OF 32 A + BC ===> BO



A BC (30)



BO
YIELD 39%

RX(30) RCT A 357292-85-4

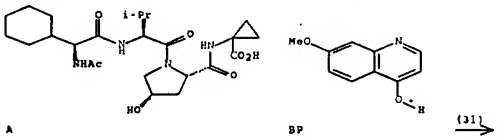
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BC 130-16-5
SOL 109-99-9 THF

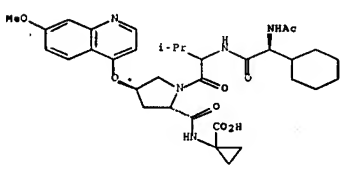
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BO 357293-15-3
NTE stereoselective, solid-supported reactant, Wang resin used

RX(31) OF 32 A + BP ===> BQ



A BP (31)



BQ

RX(31) RCT A 357292-85-4

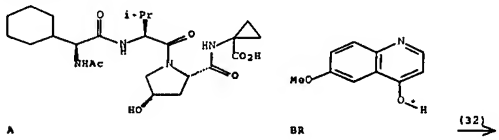
STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BP 82121-05-9
SOL 109-99-9 THF

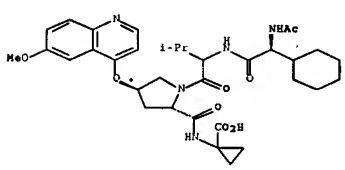
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BQ 357293-16-4
NTE stereoselective, solid-supported reactant, Weng resin used

RX(32) OF 32 A + BR ===> BS



A BR (32)



BS

RX(32) RCT A 357292-85-4

STAGE(1)
RGT D 603-35-0 PPh3, E 2446-83-5 N2(CO2CHMe2)2
SOL 75-09-2 CH2Cl2, 109-99-9 THF

STAGE(2)
RCT BR 23432-39-5
SOL 109-99-9 THF

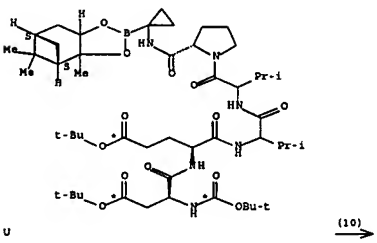
STAGE(3)
RGT F 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

PRO BS 357293-17-5
NTE stereoselective, solid-supported reactant, Wang resin used

L12 ANSWER 8 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 133:335259 CASREACT Full-text
TITLE: 1-Aminocyclopropaneboronic Acid: Synthesis and Incorporation into an Inhibitor of Hepatitis C Virus NS3 Protease
AUTHOR(S): Priestley, E. Scott; Decicco, Carl P.
CORPORATE SOURCE: Department of Chemical and Physical Sciences, DuPont Pharmaceuticals Company, Wilmington, DE, 19880, USA
SOURCE: Organic Letters (2000), 2(20), 3095-3097
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English
AB The previously unreported α,α-disubstituted 1-aminoboronate esters have potential utility in peptidomimetic design, particularly egeinst serine protease targets. A concise synthesis of 1-aminocyclopropaneboronate pinanediol ester is reported, and a peptidyl derivative has modest affinity (Ki = 1.6 μM) for hepatitis C NS3 protease. Analogs with iso-Pr and cyclohexyl in place of cyclopropyl were also prepared and tested.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(10) OF 27 ...U ===> Y



U (10)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(10) RCT U 303191-77-7
RGT P 7647-01-0 HCl
PRO Y 303191-80-2
SOL 123-91-1 Dioxane

RX(12) OF 27 AB ===> AC

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

AB

(12)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

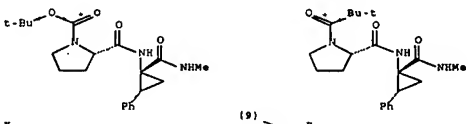
RX(12) RCT AB 303191-79-9
RGT P 7647-01-0 HCl
PRO AC 303191-82-4
SOL 123-91-1 Dioxane

L12 ANSWER 9 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 127:331716 CASREACT Full-text
TITLE: Folding types of dipeptides containing the diastereoisomeric cyclopropenic analogs of phenylalanine
AUTHOR(S): Jimenez, Ana I.; Vanderesse, Regis; Marraud, Michel; Aubry, Andre; Cativiela, Carlos
CORPORATE SOURCE: Unite de Recherche Associee au CNRS, Laboratoire de Chimie Physique Macromoleculeire ENSIC-INPL, Nancy, 54001, Fr.
SOURCE: Tetrahedron Letters (1997), 38(43), 7559-7562
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

I

AB In order to consider the possible influence of the orientation of a side chain on the peptide backbone, the mol. structure of four model dipeptides Piv-Pro-c3Pha-NHMe (Piv = Me3CCO; c3Phe = 2,3-methanophenylalanine residue I) were studied by IR and 1H NMR. All four derivs. are β-folded, but the folding type depends on the stereochem. of the cyclopropane moiety.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(9) OF 24 ...K ===> P

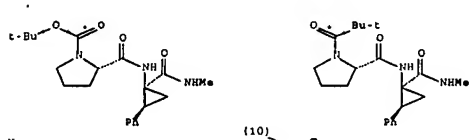


K (9) P

RX(9) RCT K 197778-19-1
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4

N-Methylmorpholine
PRO P 197778-08-8
SOL 75-09-2 CH2Cl2

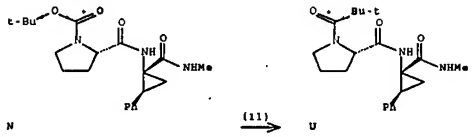
RX(10) OF 24 ...M ===> T



M T

RX(10) RCT M 197778-20-4
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO T 197778-09-9
SOL 75-09-2 CH2Cl2

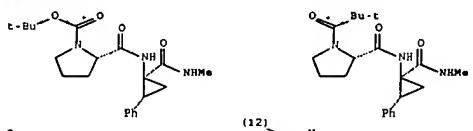
RX(11) OF 24 ...N ===> U



N U

RX(11) RCT N 197778-21-5
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO U 197778-12-4
SOL 75-09-2 CH2Cl2

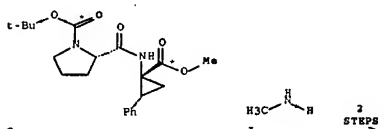
RX(12) OF 24 ...O ===> V



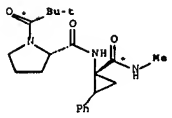
O V

RX(12) RCT O 197778-22-6
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO V 197778-13-5
SOL 75-09-2 CH2Cl2

RX(17) OF 24 COMPOSED OF RX(5), RX(9)
RX(17) C + J ===> P



C J

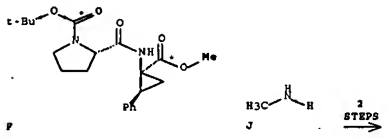


P

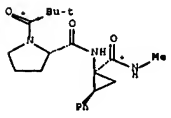
RX(5) RCT C 197778-16-8, J 74-89-5
PRO K 197778-19-1
SOL 67-56-1 MeOH

RX(9) RCT K 197778-19-1
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO P 197778-08-8
SOL 75-09-2 CH2Cl2

RX(18) OF 24 COMPOSED OF RX(6), RX(10)
RX(18) F + J ===> T



F J

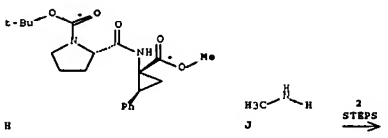


T

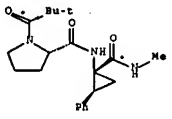
RX(6) RCT F 197778-17-9, J 74-89-5
PRO M 197778-20-4
SOL 67-56-1 MeOH

RX(10) RCT M 197778-20-4
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO T 197778-09-9
SOL 75-09-2 CH2Cl2

RX(19) OF 24 COMPOSED OF RX(7), RX(11)
RX(19) H + J ===> U



H J

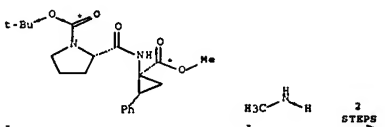


U

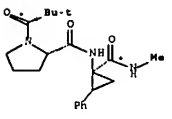
RX(7) RCT H 213996-57-7, J 74-89-5
PRO N 197778-21-5
SOL 67-56-1 MeOH

RX(11) RCT N 197778-21-5
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO U 197778-12-4
SOL 75-09-2 CH2Cl2

RX(20) OF 24 COMPOSED OF RX(8), RX(12)
RX(20) I + J ===> V



I J



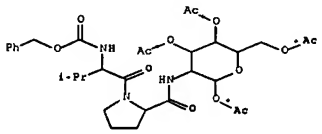
V

RX(8) RCT I 213996-58-6, J 74-89-5
PRO O 197778-22-6
SOL 67-56-1 MeOH

RX(12) RCT O 197778-22-6
RGT Q 74-87-3 MeCl, R 76-05-1 F3CCO2H, D 109-02-4
N-Methylmorpholine
PRO V 197778-13-5
SOL 75-09-2 CH2Cl2

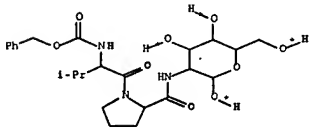
L12 ANSWER 10 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 116:230602 CASREACT Full-text
TITLE: Synthesis and properties of D-glucosamine N-peptidyl derivatives as substrate analog inhibitors of papain and cathepsin B
AUTHOR(S): Giordano, C.; Gallina, C.; Consalvi, V.; Scandurra, R.
CORPORATE SOURCE: Cent. Stud. Chim. Farm., Univ. La Sapienza, Rome, 00185, Italy
SOURCE: European Journal of Medicinal Chemistry (1991), 26(8), 753-62
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N-Peptidyl deriva. of D-glucosamina were synthesized and tested as reversible, substrate analog inhibitors of cysteine and serine proteases. D-Glucosamine itself showed fair inhibiting properties against cysteine proteases. Deriva. designed to improved binding at the papain active site, displayed reversible inhibition with Ki 67-860 μM for papain and 111-2400 μM for cathepsin B. Representative serine proteases were unaffected. No inhibitory activity against human leukocyte elastase was observed for 2 deriva. bearing very effective peptidyl recognizing units for this enzyme.

RX(15) OF 26 ...O ===> X



O

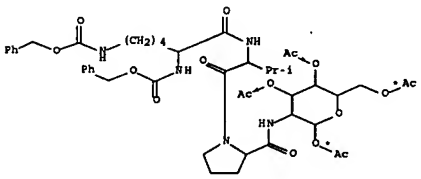
(15)



X
YIELD 70%

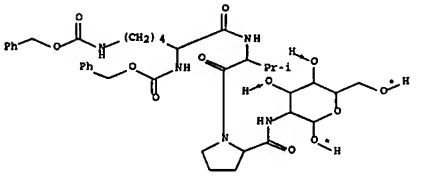
RX(15) RCT O 141280-20-8
PRO X 141266-00-4

RX(16).OF 26 ...Q ===> Y



Q

(16)



Y
YIELD 71%

RX(16) RCT Q 141280-21-9
PRO Y 141266-01-5

=> d cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	14.43	21.99
NETWORK CHARGES	2.22	3.42
SEARCH CHARGES	116.94	231.96
DISPLAY CHARGES	82.06	88.79
FULL ESTIMATED COST	215.65	346.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.49	-10.22

IN FILE 'CASREACT' AT 08:51:09 ON 30 MAY 2007

=> d hist

(FILE 'HOME' ENTERED AT 08:18:24 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 08:18:37 ON 30 MAY 2007
L1 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:19:13 ON 30 MAY 2007
L2 0 S L1 SSS SAM
L3 1 S L1 SSS FULL

FILE 'REGISTRY' ENTERED AT 08:21:37 ON 30 MAY 2007
L4 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:21:56 ON 30 MAY 2007
L5 50 S L4

FILE 'CASREACT' ENTERED AT 08:24:06 ON 30 MAY 2007
L6 28 S L5 NOT PY>2003

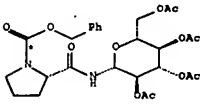
FILE 'REGISTRY' ENTERED AT 08:28:44 ON 30 MAY 2007
L7 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 08:29:13 ON 30 MAY 2007
L8 5 S L7
L9 3 S L8 NOT PY > 2003
L10 46 S L7 SSS FULL
L11 21 S L10 NOT PY >2003
L12 18 S L11 NOT L9

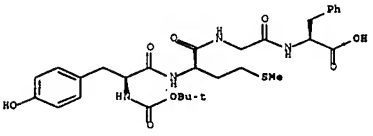
=> d ibib abs hit 11-18

L12 ANSWER 11 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 111:115724 CASREACT Full-text
TITLE: The incorporation of sugar moieties to neuropeptides: comparative study of different methods
AUTHOR(S): Torres, J. L.; Haro, I.; Bardaji, E.; Valencia, G.; Garcia-Anton, J. M.; Reig, F.
CORPORATE SOURCE: Dep. Biol. Org. Chem., CSIC, Barcelona, 08034, Spain
SOURCE: Tetrahedron (1988), 44(19), 6131-6
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By using both β-N-glycosylation and β-O-glycosylation procedures, different methods for the incorporation of glucose moieties to proline-, hydroxyproline- or glutamic acid-containing protected neuropeptides have been examined As far as glycosylation of Glu and Hyp containing fragments is concerned, the incorporation of either γ-β-N-glucosylated glutamic acid or 4-β-O-glucosylated hydroxyproline to the rest of the peptide have been chosen. However, in the case of C-terminal proline containing peptide fragments, direct β-N-glucosylation of the full peptide has been preferred. Acetyl protecting groups on the sugar moiety led to better yields than the bulkier benzyl groups.

RX(7) OF 41 ...M + S ===> R

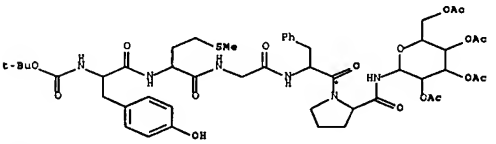


M



S

(7)



R
YIELD 5%

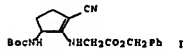
RX(7) RCT M 122350-58-7

STAGE(1)
RGT T 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

STAGE(2)
RCT S 115615-64-0
RGT E 538-75-0 DCC, F 2592-95-2 1-Benzotriazolol

PRO R 115730-55-7

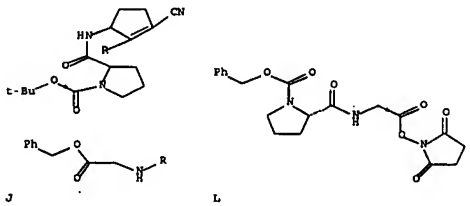
L12 ANSWER 12 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 109:6942 CASREACT Full-text
TITLE: Amino acid derivatives that stabilize secondary structures of polypeptides. III. β-Enamino nitriles as analogs of secondary amides. The MCC group [1-(acylamino)-2-(aminoalkyl)-3-cyano-2-cyclopentenes] as amino acid analogs
AUTHOR(S): Kemp, D. S.; Carter, Jeffery S.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Tetrahedron Letters (1987), 28(40), 4641-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

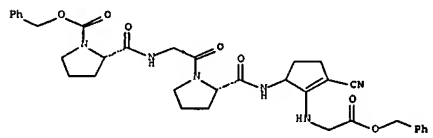
AB The properties of β-cyanoenamines as analogs of amides are studied with derivs. of a rigid amino acid equivalent I (Boc = Me3CO2C), i.e., Boc-DL-Mcc-CH2CO2CH2Ph, prepared in two steps from Me 2-(N-Boc-amino)-5- cyanopentanoate. Racemation of Mcc and incorporation into cyclic pentapeptide cyclo(Pro-Gly-Pro-DL-Mcc-Gly) are described.

RX(4) OF 21 ...J + L ===> N...



J L

(4)



M
YIELD 61%

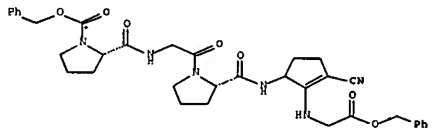
RX(4) RCT J 114542-73-3

STAGE(1)
RGT K 76-05-1 F3CCO2H, H 75-09-2 CH2Cl2

STAGE(2)
RCT L 36254-59-8

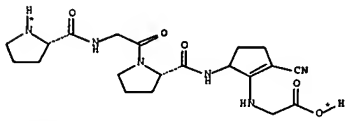
PRO M 114542-74-4

RX(5) OF 21 ...M ===> N...



M

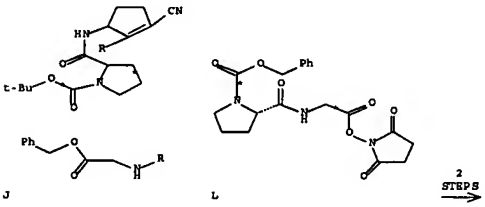
(5)



N
YIELD 93%

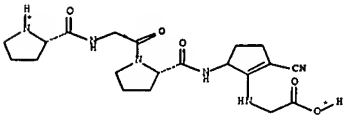
RX(5) RCT M 114542-74-4
RGT O 1333-74-0 H2
PRO N 114518-88-6
CAT 7440-05-3 Pd
SOL 64-19-7 AcOH

RX(10) OF 21 COMPOSED OF RX(4), RX(5)
RX(10) J + L ===> N



J L

2 STEPS



N
YIELD 93%

RX(4) RCT J 114542-73-3

STAGE(1)
RGT K 76-05-1 F3CCO2H, H 75-09-2 CH2Cl2

STAGE(2)
RCT L 36254-59-8

PRO M 114542-74-4

RX(5) RCT M 114542-74-4
RGT O 1333-74-0 H2
PRO N 114518-88-6
CAT 7440-05-3 Pd

SOL 64-19-7 AcOH

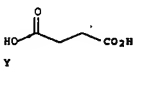
L12 ANSWER 13 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 108:112956 CASREACT Full-text
TITLE: Preparation of amino acid and peptide arylamides as chromogenic reagents in enzyme determinations
INVENTOR(S): Bajusz, Sandor; Juhasz, Attila; Barabas, Eva; Bagdi, Daniel; Mohai, Laszlo, Mrs.
PATENT ASSIGNEE(S): Gyogyszerkutato Intezet, Hung.
SOURCE: Hung. Teljes, 37 pp.
CODEN: HUXXBU
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 40615	A2	19870128	HU 1985-2330	19850613
HU 198172	B	19890828		
SU 1512484	A3	19890930	SU 1986-4028098	19860908

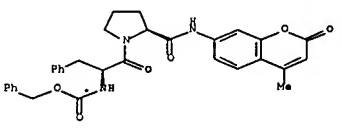
PRIORITY APPLN. INFO.: HU 1985-2330 19850613

AB The title compds. RXA (R = H, acyl, aminoacyl, acylaminoacyl, peptidyl, acylpeptidyl; X = L-α-amino acid radical; A = p-nitroanilino, 4-methylcoumarinyl-7-amino) are prepared by reacting the protected corresponding amino acid or peptide with PCl3 and the aryl amide, in <0.2% water-containing pyridine, followed by deprotection. The arylamine/PCl3 mol. ratio is 1:0.6-1.5, which is more PCl3 than the conventional amount A solution of 6.8 g N2-tert-butyloxycarbonyl-L-arginine-HCl.H2O and 2.8 g p-nitroaniline in 20 mL pyridine, was treated, at -20°, with 2.26 mL PCl3, to give N2-tert-butyloxycarbonyl-L-arginine-p-nitroanilide- HCl.H2O, which was treated with HCl in EtOAc to give L-arginine-p-nitroanilide-2HCl.H2O. The products are chromogenic and fluorogenic reagents in the determination of proteases and transpeptidases.

RX(16) OF 67 ...Y + X ===> Z

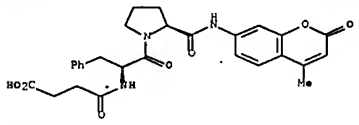


Y



X

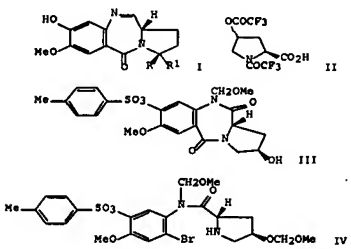
(16)



Z
YIELD 90%

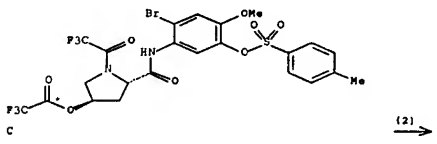
RX(16) RCT Y 110-15-6, X 113277-38-6
PRO Z 113277-36-4

L12 ANSWER 14 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 106:18224 CASREACT Full-text
TITLE: Total synthesis of neothramycin
AUTHOR(S): Mori, Miwako; Uozumi, Yasuhiro; Ban, Yoshio
CORPORATE SOURCE: Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (11), 841-2
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



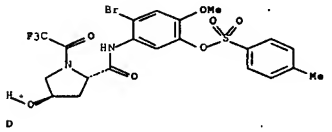
AB Neothramycin A and B (I; R = H, R1 = OH; R = OH, R1 = H, resp.), from Streptomyces, were prepared in 12 steps from 5,4,2-(4- MeC6H4SO3)(MeO)BrC6H2NH2 and the hydroxyproline II, via the key intermediate III, which was obtained by Pd(PPh3)4-catalyzed carbonylation of the secondary amine IV followed by deprotection.

RX(2) OF 112 ...C ===> D...



C

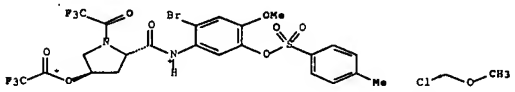
(2)



D

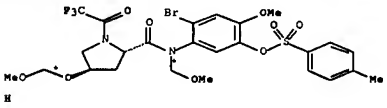
RX(2) RCT C 105842-35-1
RGT E 144-55-8 NaHCO3
PRO D 105823-07-2
SOL 7732-18-5 Water

RX(18) OF 112 COMPOSED OF RX(2), RX(3)
RX(18) C + 2 G ===> H



C 2 G

2
STEPS



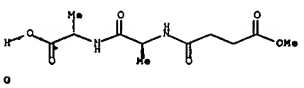
H

RX(2) RCT C 105842-35-1
RGT E 144-55-8 NaHCO3
PRO D 105823-07-2
SOL 7732-18-5 Water

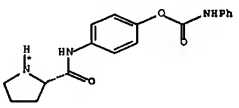
RX(3) RCT D 105823-07-2, G 107-30-2
RGT I 7087-68-5 EtN(Pr-i)2
PRO H 105823-08-3

L12 ANSWER 15 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 105:60932 CASREACT Full-text
TITLE: Peptidyl carbamates incorporating amino acid isosteres as novel elastase inhibitors
AUTHOR(S): Digenis, George A.; Agha, Bushra J.; Tsuji, Kiyoshi; Kato, Masayuki; Shinogi, Masaki
CORPORATE SOURCE: Coll. Pharm., Univ. Kentucky, Lexington, KY, 40536-0053, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(8), 1468-76
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Title peptidyl carbamates MeO2CCH2CH2CO-Ala-Ala-Pro-NHZO2CNRR1 [I; Z = p-C6H4, R = H, R1 = Ph, CHMe2; Z = p-C6H4, R = R1 = Me; Z = o-C6H4, CH(CHMe2)CH2, R = H, R1 = Ph] and MeO2CCH2CH2CO-Ala-Ala-Pro- CH2N(CHMe2)COXR2 [II; X = O, R2 = C6H4NO2-p, Ph, C6F5, CH2CF2CF2CF3; X = S, R2 = CH2Ph, 1-methyl-5-tetrazolyl, 1-phenyl-5-tetrazolyl] were prepared and they were tested as inhibitors of elastase, trypsin, and chymotrypsin. Thus, Boc-Pro-NHZOH (Boc = Me3CO2C) were treated with RR1NCOCl or RR1NCO to give Boc-Pro-NHZO2CNRR1, which were Boc-deblocked and then coupled with MeO2CCH2CH2CO-Ala-Ala-OH (III) by ClCO2CH2CHMe2 to give I. Boc-Pro-CH2Cl was treated with H2NCHMe2 to give Boc-Pro-CH2NHCHMe2, which was treated with R2XCOCl to give Boc-Pro-CH2N(CHMe2)COXR2, which were Boc-deblocked and then coupled with III to give II. Six peptidyl carbamates specifically inhibited elastase without affecting trypsin and chymotrypsin. Kinetic studies showed that the inhibition was competitive. The inhibition is reversible and proceeds via the rapid formation of a strong enzyme-inhibitor complex, followed by slow acylation of the serine residue on the active site of the enzyme.

RX(16) OF 173 ...G + AE ===> AL



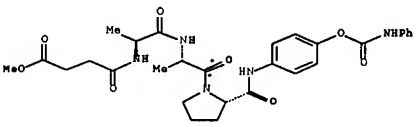
G



● HCl

AE

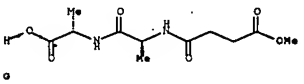
(16)



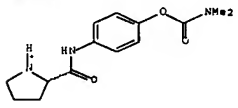
AL

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(17) OF 173 ...G + AH ===> AO



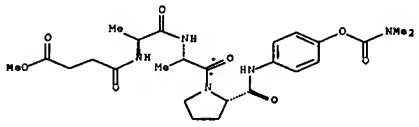
G



● HCl

AH

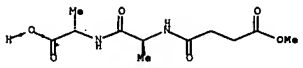
(17) →



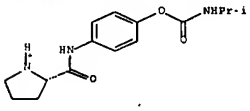
AO

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(18) OF 173 ...G + AI ===> AQ



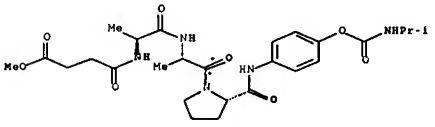
G



● HCl

AI

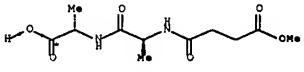
(18) →



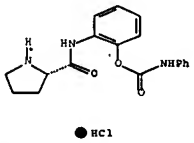
AQ

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(19) OF 173 ...G + AJ ===> AR



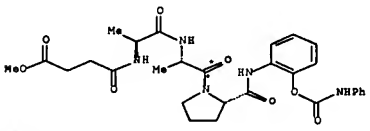
G



● HCl

AJ

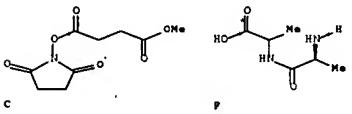
(19) →



AR

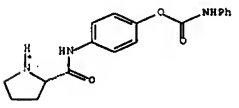
RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(42) OF 173 COMPOSED OF RX(2), RX(16)
RX(42) C + F + AE ===> AL



C

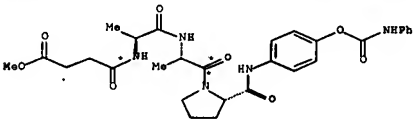
F



● HCl

AE

2 STEPS →

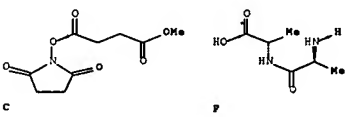


AL

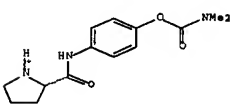
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(43) OF 173 COMPOSED OF RX(2), RX(17)
RX(43) C + F + AH ===> AO



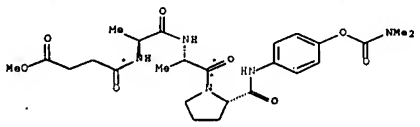
C F



● HCl

AH

2 STEPS →

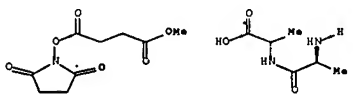


AO

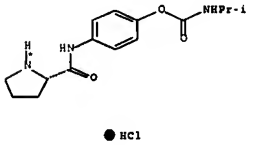
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(44) OF 173 COMPOSED OF RX(2), RX(18)
RX(44) C + F + AI ===> AQ



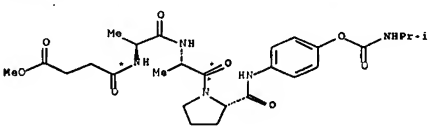
C F



● HCl

AI

2 STEPS

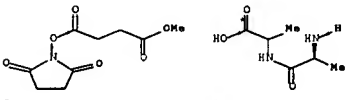


AQ

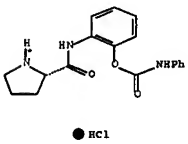
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(45) OF 173 COMPOSED OF RX(2), RX(19)
RX(45) C + F + AJ ===> AR



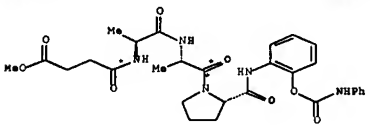
C F



● HCl

AJ

2 STEPS

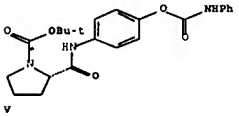


AR

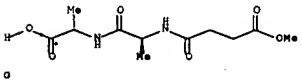
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(64) OF 173 COMPOSED OF RX(11), RX(16)
RX(64) V + G ===> AL

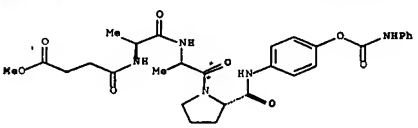


V



G

2 STEPS

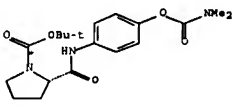


AL

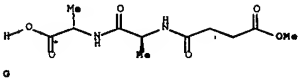
RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(65) OF 173 COMPOSED OF RX(12), RX(17)
RX(65) Z + G ===> AO

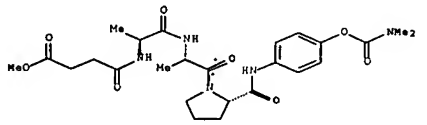


Z



G

2 STEPS

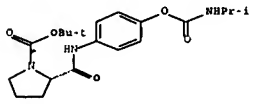


AO

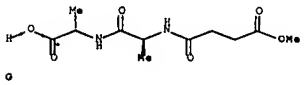
RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(66) OF 173 COMPOSED OF RX(13), RX(16)
RX(66) AB + G ===> AO

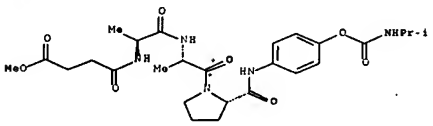


AB



G

2 STEPS

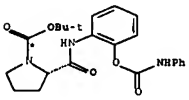


AQ

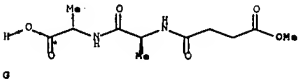
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(67) OF 173 COMPOSED OF RX(14), RX(19)
RX(67) AC + G ===> AR

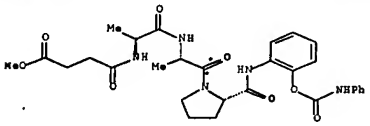


AC



G

2 STEPS

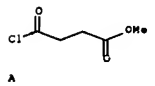


AR

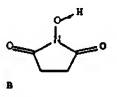
RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

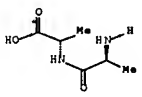
RX(81) OF 173 COMPOSED OF RX(1), RX(2), RX(16)
RX(81) A + B + F + AE ===> AL



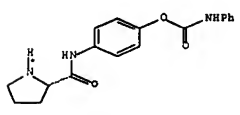
A



B



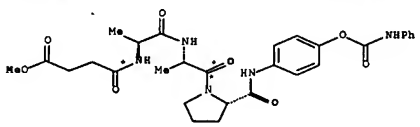
F



AE

● HCl

3 STEPS



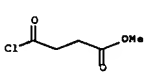
AL

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

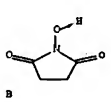
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

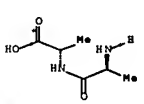
RX(82) OF 173 COMPOSED OF RX(1), RX(2), RX(17)
RX(82) A + B + F + AH ===> AO



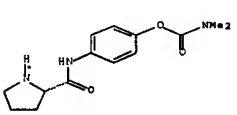
A



B



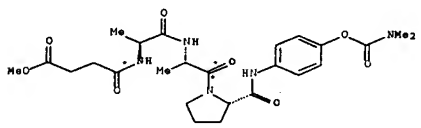
F



AH

● HCl

3 STEPS



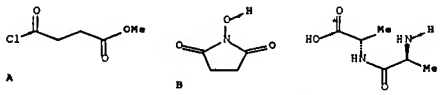
AO

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

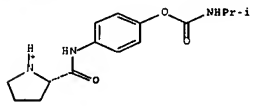
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(83) OF 173 COMPOSED OF RX(1), RX(2), RX(18)
RX(83) A + B + F + AI ===> AQ



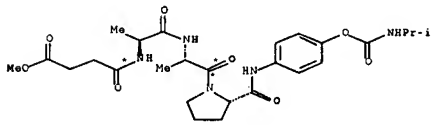
A B F



● HCl

AI

3 STEPS



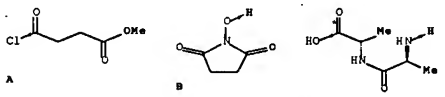
AQ

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

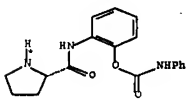
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(84) OF 173 COMPOSED OF RX(1), RX(2), RX(19)
RX(84) A + B + F + AJ ===> AR



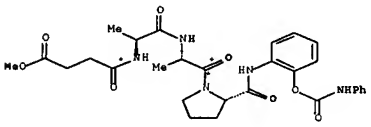
A B F



● HCl

AJ

3 STEPS



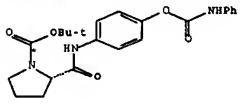
AR

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

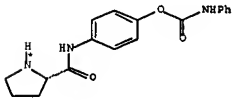
RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(93) OF 173 COMPOSED OF REACTION SEQUENCE RX(11), RX(16)
AND REACTION SEQUENCE RX(2), RX(16)
...V ===> AE...
... C + F + AE ===> AL



V

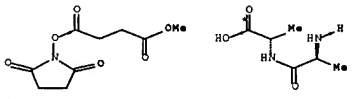
2 STEPS



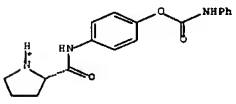
● HCl

AE

START NEXT REACTION SEQUENCE



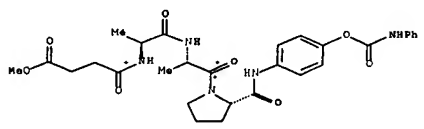
C F



● HCl

AE

2 STEPS



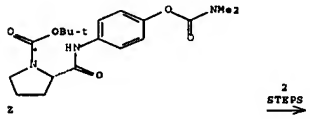
AL

RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

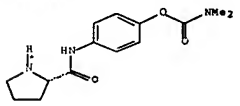
RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(94) OF 173 COMPOSED OF REACTION SEQUENCE RX(12), RX(17)
AND REACTION SEQUENCE RX(2), RX(17)
...Z ===> AH...
... C + F + AH ===> AO



Z

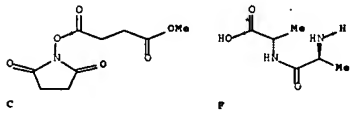
2 STEPS



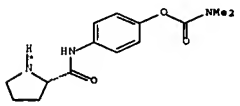
● HCl

AH

START NEXT REACTION SEQUENCE



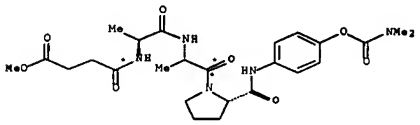
C F



● HCl

AH

2 STEPS



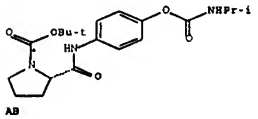
AO

RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

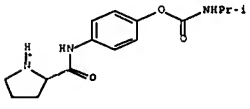
RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(95) OF 173 COMPOSED OF REACTION SEQUENCE RX(13), RX(18)
AND REACTION SEQUENCE RX(2), RX(18)
...AB ===> AI...
... C + F + AI ===> AQ



AB

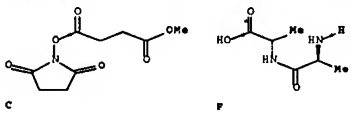
2 STEPS



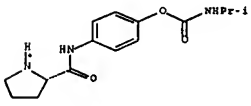
● HCl

AI

START NEXT REACTION SEQUENCE



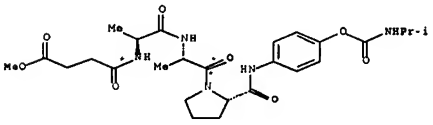
C F



● HCl

AI

2 STEPS



AQ

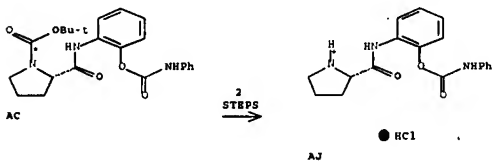
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

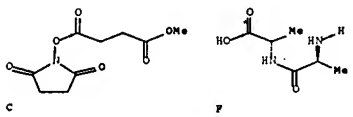
RX(96) OF 173 COMPOSED OF REACTION SEQUENCE RX(14), RX(19)
AND REACTION SEQUENCE RX(2), RX(19)

...AC ===> AJ...
... C + F + AJ ===> AR

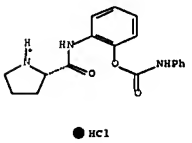


AC AJ

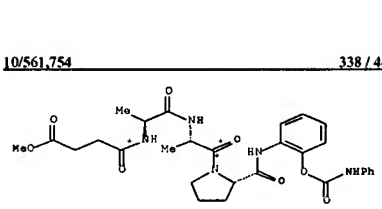
START NEXT REACTION SEQUENCE



C F



AJ



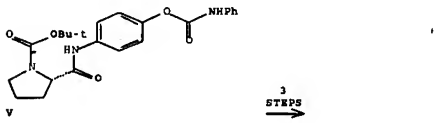
AR

RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

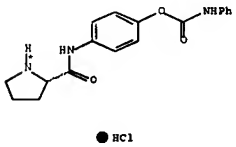
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(102) OF 173 COMPOSED OF REACTION SEQUENCE RX(11), RX(16)
AND REACTION SEQUENCE RX(1), RX(2), RX(16)
...V ===> AE...
... A + B + F + AE ===> AL

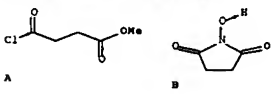


V

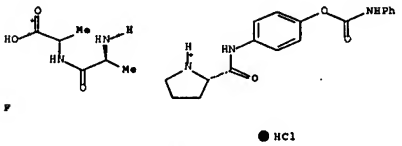


AE

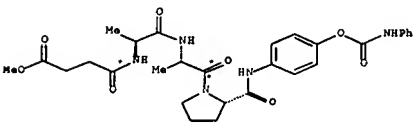
START NEXT REACTION SEQUENCE



A B



F AE



AL

RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

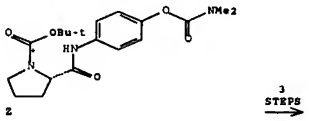
RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

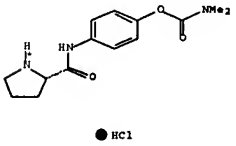
RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine

PRO AL 92279-27-1
SOL 109-99-9 THF

RX(103) OF 173 COMPOSED OF REACTION SEQUENCE RX(12), RX(17)
AND REACTION SEQUENCE RX(1), RX(2), RX(17)
...Z ===> AH...
... A + B + F + AH ===> AO

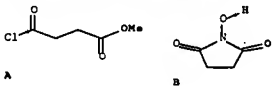


Z

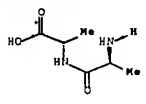


AH

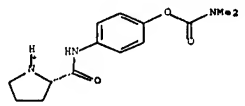
START NEXT REACTION SEQUENCE



A B



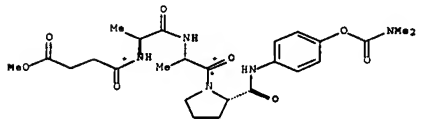
F



● HCl

AH

3 STEPS



AO

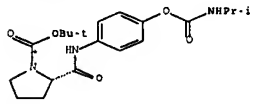
RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

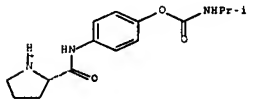
RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(104) OF 173 COMPOSED OF REACTION SEQUENCE RX(13), RX(18) AND REACTION SEQUENCE RX(1), RX(2), RX(18)
...AB ===> AI...
... A + B + F + AI ===> AQ



AB

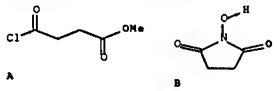
3 STEPS



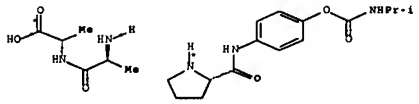
● HCl

AI

START NEXT REACTION SEQUENCE



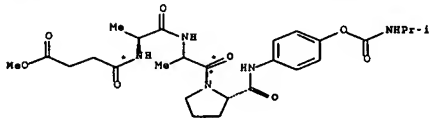
A B



F AI

● HCl

3 STEPS



AQ

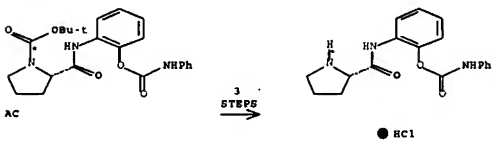
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(105) OF 173 COMPOSED OF REACTION SEQUENCE RX(14), RX(19) AND REACTION SEQUENCE RX(1), RX(2), RX(19)
...AC ===> AJ...
... A + B + F + AJ ===> AR



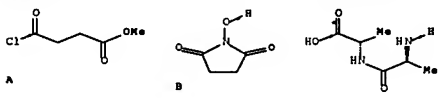
AC

3 STEPS

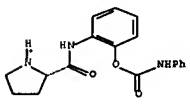
● HCl

AJ

START NEXT REACTION SEQUENCE



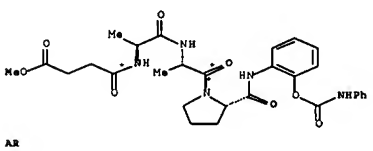
A B F



● HCl

AJ

3 STEPS



AR

RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

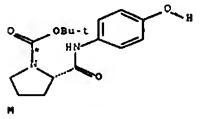
RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

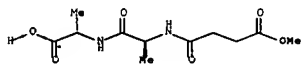
RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i

PRO AR 92279-30-6

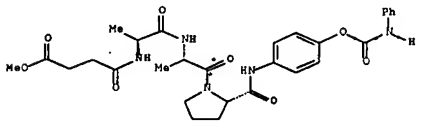
RX(116) OF 173 COMPOSED OF RX(6), RX(11), RX(16)
RX(116) M + U + G ===> AL


M


U


G

3 STEPS

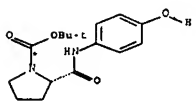

AL

RX(6) RCT M 102284-28-6, U 103-71-9
RGT W 110-86-1 Pyridine
PRO V 102284-31-1
SOL 68-12-2 DMF

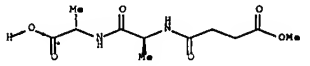
RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

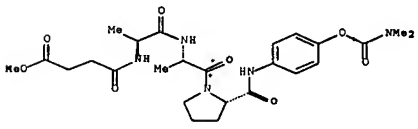
RX(118) OF 173 COMPOSED OF RX(7), RX(12), RX(17)
RX(118) M + Y + G ===> AO


M


Y


G

3 STEPS

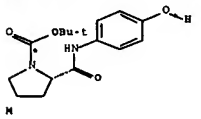

AO

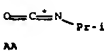
RX(7) RCT M 102284-28-6, Y 79-44-7
PRO Z 102284-32-2
SOL 110-86-1 Pyridine

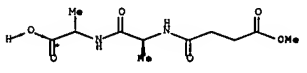
RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

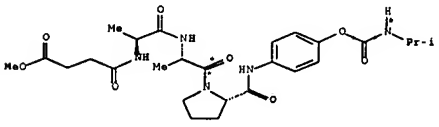
RX(120) OF 173 COMPOSED OF RX(8), RX(13), RX(18)
RX(120) M + AA + G ===> AQ


M


AA


G

3 STEPS

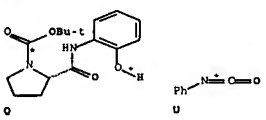

AQ

RX(8) RCT M 102284-28-6, AA 1795-48-8
RGT W 110-86-1 Pyridine
PRO AB 102284-33-3
SOL 68-12-2 DMF

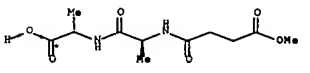
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

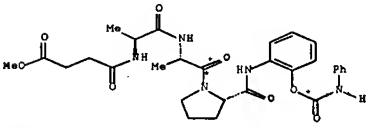
RX(122) OF 173 COMPOSED OF RX(9), RX(14), RX(19)
RX(122) Q + U + G ===> AR


Q

U


G

3 STEPS

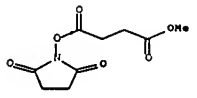

AR

RX(9) RCT Q 102284-29-7, U 103-71-9
PRO AC 102284-34-4

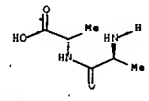
RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(126) OF 173 COMPOSED OF REACTION SEQUENCE RX(2), RX(16)
AND REACTION SEQUENCE RX(6), RX(11), RX(16)
...C + F ===> G...
... M + U + G ===> AL

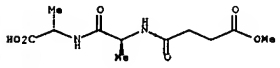


C



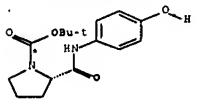
F

3 STEPS



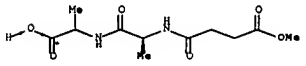
G

START NEXT REACTION SEQUENCE



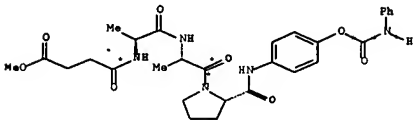
M

U



G

3 STEPS



AL

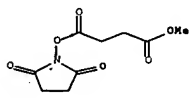
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(6) RCT M 102284-28-6, U 103-71-9
RGT W 110-86-1 Pyridine
PRO V 102284-31-1
SOL 68-12-2 DMF

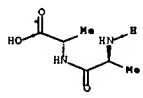
RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(127) OF 173 COMPOSED OF REACTION SEQUENCE RX(2), RX(17)
AND REACTION SEQUENCE RX(7), RX(12), RX(17)
...C + F ===> G...
... M + Y + G ===> AO

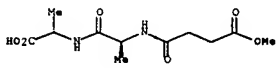


C



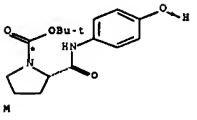
F

3 STEPS



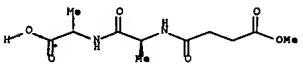
G

START NEXT REACTION SEQUENCE



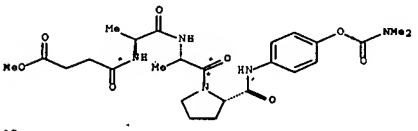
M

Y



G

3 STEPS



AO

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

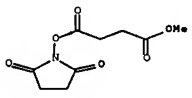
RX(7) RCT M 102284-28-6, Y 79-44-7
PRO Z 102284-32-2
SOL 110-86-1 Pyridine

RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

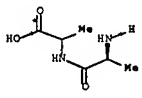
RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(128) OF 173 COMPOSED OF REACTION SEQUENCE RX(2), RX(18)

AND REACTION SEQUENCE RX(8), RX(13), RX(18)
...C + F ===> G...
... M + AA + G ===> AQ

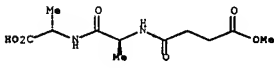


C



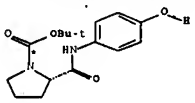
F

3 STEPS

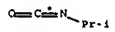


G

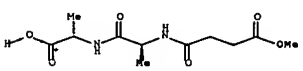
START NEXT REACTION SEQUENCE



M

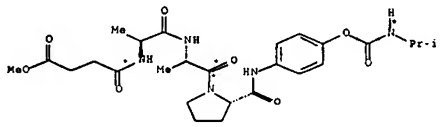


AA



G

3 STEPS



AQ

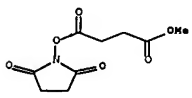
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(8) RCT M 102284-28-6, AA 1795-48-8
RGT W 110-86-1 Pyridine
PRO AB 102284-33-3
SOL 68-12-2 DMF

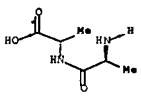
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(129) OF 173 COMPOSED OF REACTION SEQUENCE RX(2), RX(13)
AND REACTION SEQUENCE RX(9), RX(14), RX(19)
...C + F ===> G...
... Q + U + G ===> AR

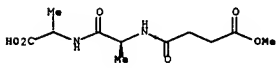


C



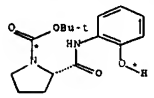
F

3 STEPS

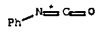


G

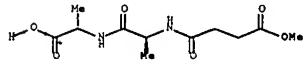
START NEXT REACTION SEQUENCE



Q

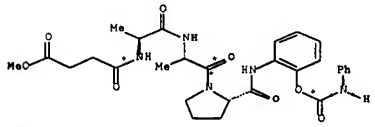


U



G

3 STEPS



AR

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

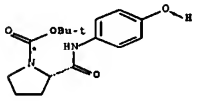
RX(9) RCT Q 102284-29-7, U 103-71-9
PRO AC 102284-34-4

RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(147) OF 173 COMPOSED OF REACTION SEQUENCE RX(6), RX(11), RX(16)
AND REACTION SEQUENCE RX(1), RX(2), RX(16)

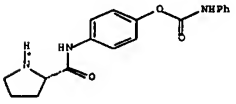
...M + U ===> AE...
... A + B + F + AE ===> AL



M

U

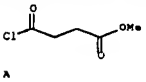
3 STEPS



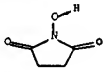
● HCl

AE

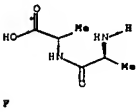
START NEXT REACTION SEQUENCE



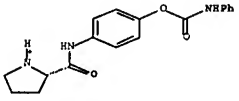
A



B



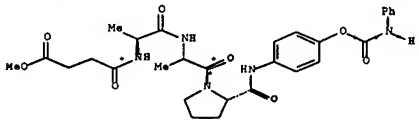
F



● HCl

AE

3 STEPS



AL

RX(6) RCT M 102284-28-6, U 103-71-9
RGT W 110-86-1 Pyridine
PRO V 102284-31-1
SOL 68-12-2 DMF

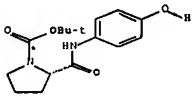
RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

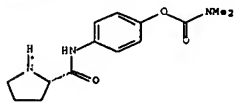
RX(148) OF 173 COMPOSED OF REACTION SEQUENCE RX(7), RX(12), RX(17)
AND REACTION SEQUENCE RX(1), RX(2), RX(17)
...M + Y ===> AH...
... A + B + F + AH ===> AO



M

Y

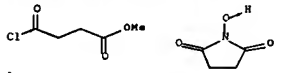
3 STEPS



● HCl

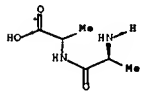
AH

START NEXT REACTION SEQUENCE

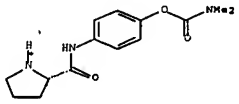


A

B



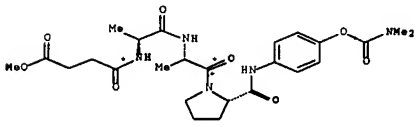
F



● HCl

AH

3 STEPS



AO

RX(7) RCT M 102284-28-6, Y 79-44-7
PRO Z 102284-32-2

SOL 110-86-1 Pyridine

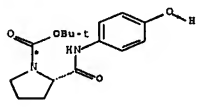
RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

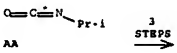
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine,. AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(149) OF 173 COMPOSED OF REACTION SEQUENCE RX(8), RX(13), RX(18) AND REACTION SEQUENCE RX(1), RX(2), RX(18)
...M + AA ===> AI...
... A + B + F + AI ===> AQ

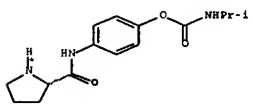


M



AA

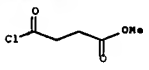
3 STEPS



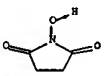
● HCl

AI

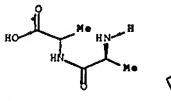
START NEXT REACTION SEQUENCE



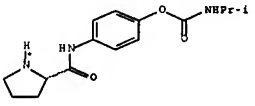
A



B



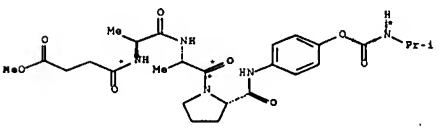
F



● HCl

AI

3 STEPS



AQ

RX(8) RCT M 102284-28-6, AA 1795-48-8
RGT W 110-86-1 Pyridine
PRO AB 102284-33-3
SOL 68-12-2 DMF

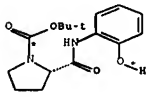
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

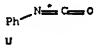
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(150) OF 173 COMPOSED OF REACTION SEQUENCE RX(9), RX(14), RX(19) AND REACTION SEQUENCE RX(1), RX(2), RX(19)
...Q + U ===> AJ...
... A + B + F + AJ ===> AR

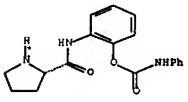


Q



U

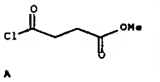
3 STEPS



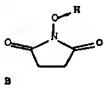
● HCl

AJ

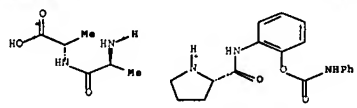
START NEXT REACTION SEQUENCE



A



B

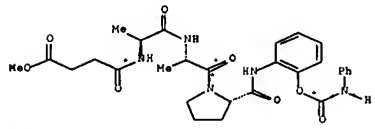


F

● HCl

AJ

3 STEPS



AR

RX(9) RCT Q 102284-29-7, U 103-71-9
PRO AC 102284-34-4

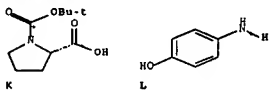
RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

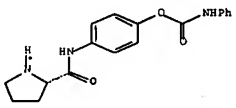
RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(154) OF 173 COMPOSED OF REACTION SEQUENCE RX(3), RX(6), RX(11), RX(16)
AND REACTION SEQUENCE RX(2), RX(16)
...K + L + U ===> AE...
... C + F + AE ===> AL



K L U

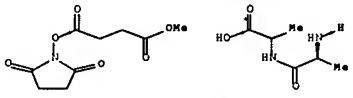
2 STEPS



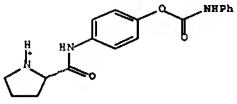
● HCl

AE

START NEXT REACTION SEQUENCE



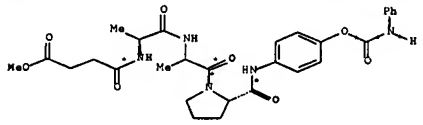
C F



● HCl

AE

2 STEPS



AL

RX(3) RCT K 15761-39-4, L 123-30-8
RGT N 538-75-0 DCC
PRO M 102284-28-6
SOL 109-99-9 THF

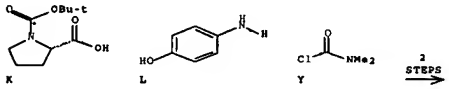
RX(6) RCT M 102284-28-6, U 103-71-9
RGT W 110-86-1 Pyridine
PRO V 102284-31-1
SOL 68-12-2 DMF

RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

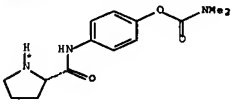
RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(155) OF 173 COMPOSED OF REACTION SEQUENCE RX(3), RX(7), RX(12), RX(17)
AND REACTION SEQUENCE RX(2), RX(17)
...K + L + Y ===> AH...
... C + F + AH ===> AO



K L Y

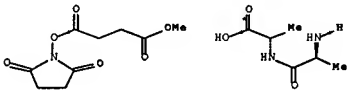
2 STEPS



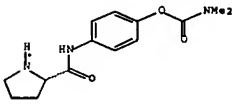
● HCl

AH

START NEXT REACTION SEQUENCE



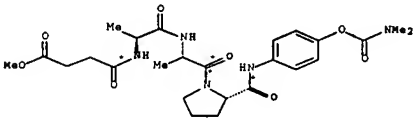
C F



● HCl

AH

2 STEPS



AO

RX(3) RCT K 15761-39-4, L 123-30-8
RGT N 538-75-0 DCC
PRO M 102284-28-6
SOL 109-99-9 THF

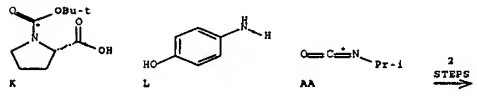
RX(7) RCT M 102284-28-6, Y 79-44-7
PRO Z 102284-32-2
SOL 110-86-1 Pyridine

RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

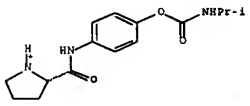
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(156) OF 173 COMPOSED OF REACTION SEQUENCE RX(3), RX(8), RX(13), RX(18) AND REACTION SEQUENCE RX(2), RX(18)
...K + L + AA ===> AI...
... C + F + AI ===> AQ

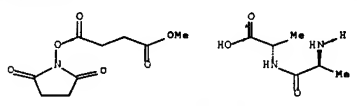


K L AA

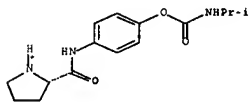


AI

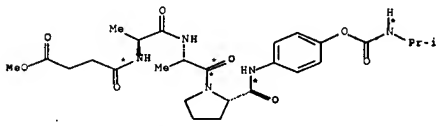
START NEXT REACTION SEQUENCE



C F



AI



AQ

RX(3) RCT K 15761-39-4, L 123-30-8
RGT N 538-75-0 DCC
PRO M 102284-28-6
SOL 109-99-9 THF

RX(8) RCT M 102284-28-6, AA 1795-48-8
RGT W 110-86-1 Pyridine
PRO AB 102284-33-3
SOL 68-12-2 DMF

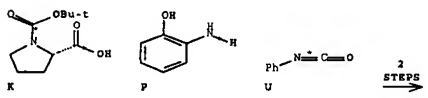
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3

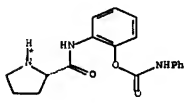
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(18) RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(157) OF 173 COMPOSED OF REACTION SEQUENCE RX(4), RX(9), RX(14), RX(19) AND REACTION SEQUENCE RX(2), RX(19)
...K + P + U ===> AJ...
... C + F + AJ ===> AR

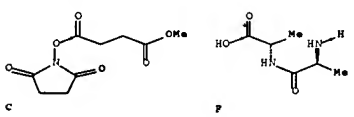


K P U

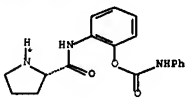


AJ

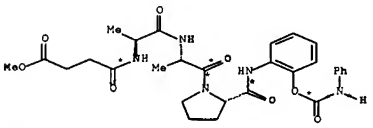
START NEXT REACTION SEQUENCE



C F



AJ



AR

RX(4) RCT K 15761-39-4, P 95-55-6
RGT N 538-75-0 DCC
PRO Q 102284-29-7
SOL 109-99-9 THF

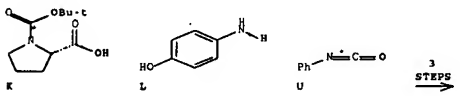
RX(9) RCT Q 102284-29-7, U 103-71-9
PRO AC 102284-34-4

RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

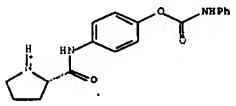
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

RX(161) OF 173 COMPOSED OF REACTION SEQUENCE RX(3), RX(6), RX(11), RX(16) AND REACTION SEQUENCE RX(1), RX(2), RX(16)
...K + L + U ===> AE...
... A + B + F + AE ===> AL



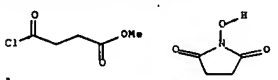
K L U



● HCl

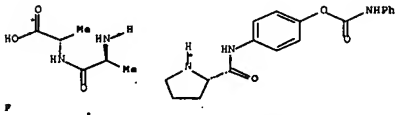
AE

START NEXT REACTION SEQUENCE



A

B

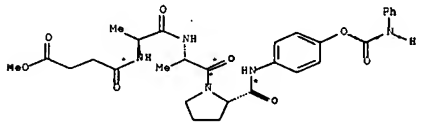


F

● HCl

AE

3
STEPS



AL

RX(3) RCT K 15761-39-4, L 123-30-8
RGT N 538-75-0 DCC
PRO M 102284-28-6
SOL 109-99-9 THF

RX(6) RCT M 102284-28-6, U 103-71-9
RGT N 110-86-1 Pyridine
PRO V 102284-31-1
SOL 68-12-2 DMF

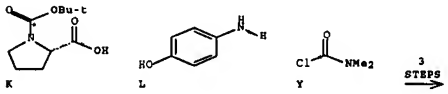
RX(11) RCT V 102284-31-1
RGT AF 7647-01-0 HCl
PRO AE 102284-36-6
SOL 109-99-9 THF, 64-18-6 HCO2H

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

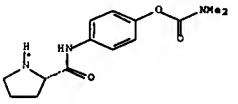
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(16) RCT G 102284-27-5, AE 102284-36-6
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine
PRO AL 92279-27-1
SOL 109-99-9 THF

RX(162) OF 173 COMPOSED OF REACTION SEQUENCE RX(3), RX(7), RX(12), RX(17)
AND REACTION SEQUENCE RX(1), RX(2), RX(17)
...K + L + Y ===> AH...
... A + B + F + AH ===> AO



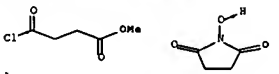
K L Y



● HCl

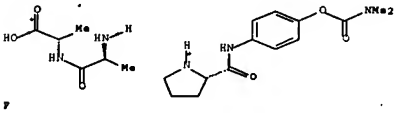
AH

START NEXT REACTION SEQUENCE



A

B

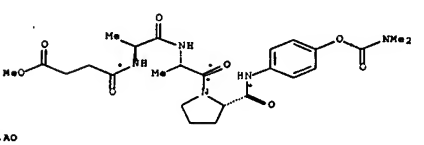


F

● HCl

AH

3
STEPS



AO

RX(3) RCT K 15761-39-4, L 123-30-8
RGT N 538-75-0 DCC
PRO M 102284-28-6
SOL 109-99-9 THF

RX(7) RCT M 102284-28-6, Y 79-44-7
PRO Z 102284-32-2
SOL 110-86-1 Pyridine

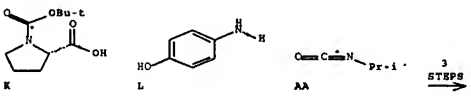
RX(12) RCT Z 102284-32-2
RGT AF 7647-01-0 HCl
PRO AH 102284-37-7

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

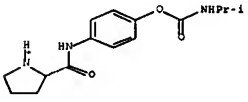
RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(17) RCT G 102284-27-5, AH 102284-37-7
RGT AM 543-27-1 ClCO2Bu-i, AN 109-02-4 N-Methylmorpholine, AP 10416-59-8 Me3SiN:CMeOSiMe3
PRO AO 92279-28-2
SOL 109-99-9 THF

RX(163) OF 173 COMPOSED OF REACTION SEQUENCE RX(3), RX(8), RX(13), RX(18)
AND REACTION SEQUENCE RX(1), RX(2), RX(18)
...K + L + AA ===> AI...
... A + B + F + AI ===> AQ



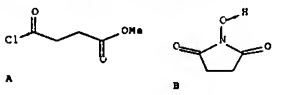
K L AA



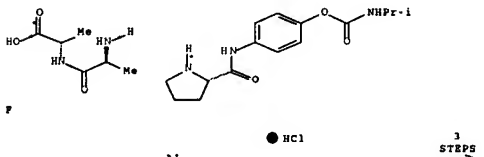
● HCl

AI

START NEXT REACTION SEQUENCE



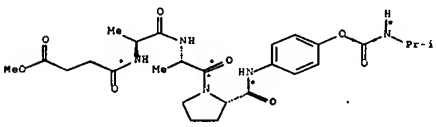
A B



F AI

● HCl

3 STEPS



AQ

RX(3) RCT K 15761-39-4, L 123-30-8
RGT N 538-75-0 DCC
PRO M 102284-28-6
SOL 109-99-9 THF

RX(8) RCT M 102284-28-6, AA 1795-48-8
RGT W 110-86-1 Pyridine
PRO AB 102284-33-3
SOL 68-12-2 DMF

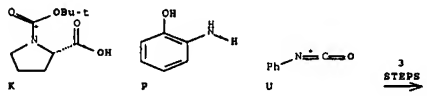
RX(13) RCT AB 102284-33-3
RGT AF 7647-01-0 HCl
PRO AI 102284-38-8

RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

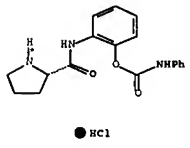
RX(18). RCT G 102284-27-5, AI 102284-38-8
RGT AM 543-27-1 ClCO2Bu-i
PRO AQ 92279-29-3

RX(164) OF 173 COMPOSED OF REACTION SEQUENCE RX(4), RX(9), RX(14), RX(19) AND REACTION SEQUENCE RX(1), RX(2), RX(19)
...K + P + U ===> AJ...
... A + B + F + AJ ===> AR



K P U

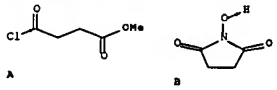
3 STEPS



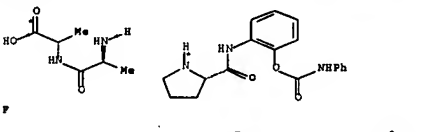
● HCl

AJ

START NEXT REACTION SEQUENCE



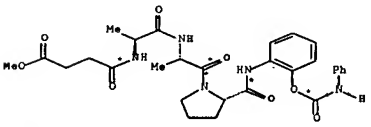
A B



F AJ

● HCl

3 STEPS



AR

RX(4) RCT K 15761-39-4, P 95-55-6
RGT N 538-75-0 DCC
PRO Q 102284-29-7
SOL 109-99-9 THF

RX(9) RCT Q 102284-29-7, U 103-71-9
PRO AC 102284-34-4

RX(14) RCT AC 102284-34-4
RGT AF 7647-01-0 HCl
PRO AJ 102284-39-9

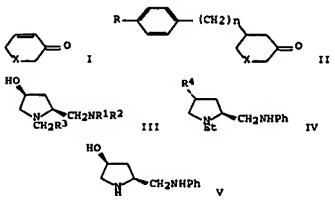
RX(1) RCT A 1490-25-1, B 6066-82-6
RGT D 121-44-8 Et3N
PRO C 52787-46-9
SOL 141-78-6 AcOEt

RX(2) RCT C 52787-46-9, F 1948-31-8
RGT H 144-55-8 NaHCO3
PRO G 102284-27-5
SOL 7732-18-5 Water, 67-64-1 Me2CO

RX(19) RCT G 102284-27-5, AJ 102284-39-9
RGT AM 543-27-1 ClCO2Bu-i
PRO AR 92279-30-6

L12 ANSWER 16 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 98:143062 CASREACT Full-text
TITLE: The enantioselective Michael addition of thiols to

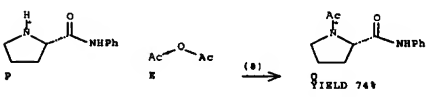
cycloalkenones by using (2S,4S)-2-(anilinomethyl)-1-ethyl-4-hydroxypyrrolidine as chiral catalyst
AUTHOR(S): Suzuki, Keisuke; Ikegawa, Akihiko; Mukaiyama, Teruaki
CORPORATE SOURCE: Fac. Sci., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Bulletin of the Chemical Society of Japan (1982), 55(10), 3277-82
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II III IV V

AB Catalytic asym. addition of thiols 4-RC6H4(CH2)nSH (R = H, Me, Cl, MeO, Me3C, n = 0; R = H, n = 1) to 2-cycloalkenones I (X = bond, CH2, CH2CH2, CMe2) to give II was studied by using the chiral amino alcs. III (R1 = H, R2 = Ph, cyclohexyl, 2,6-Me2C6H3, 1-naphthyl, R3 = Me; R1 = R3 = H, R2 = Ph; R1 = H, R2 = Ph, R3 = Me3C) IV (R4 = H, OH), and V derived from L-hydroxyproline or (S)-proline, as base catalysts. The effects of the structure of the catalyst, the reaction medium, the temperature, and the concentration on the enantioselectivity of the reaction was determined Good optical yields (47-88%) were achieved by the reaction of arenethiols and 2-cyclohexen-1-one in toluene at -5°, by using the catalyst (2S,4S)-2-anilinomethyl-1-ethyl-4-hydroxypyrrolidine.

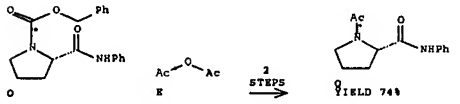
RX(8) OF 16 ...P + E ===> Q...



P E (8) Q YIELD 74%

RX(8) RCT P 64030-43-9, E 108-24-7
PRO Q 84646-41-3

RX(14) OF 16 COMPOSED OF RX(7), RX(8)
RX(14) O + E ===> Q

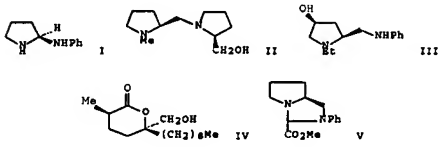


O E Q
YIELD 74%

RX(7) RCT O 64030-42-8
PRO P 64030-43-9

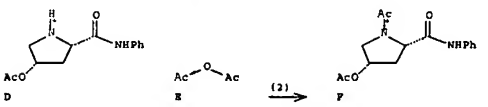
RX(8) RCT P 64030-43-9, E 108-24-7
PRO Q 64846-41-3

L12 ANSWER 17 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 97:71598 CASREACT Full-text
TITLE: Asymmetric synthesis based on chiral diamines having a pyrrolidine ring
AUTHOR(S): Mukaiyama, Teruaki
CORPORATE SOURCE: Dep. Chem., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Tetrahedron (1981), 37(23), 4111-19
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The chiral diamines I-III were used in the asym. preparation of chiral aldehydes and secondary alcs. and in enantioselective addition reactions of thiols with cyclohexenone. Treatment of I with LiAlH4 in Et2O at room temperature for 1 h followed by addition of PhCOMe in Et2O at -100° gave 87% (S)-PhCH(OH)Me. The preparation of the marine antibiotic, (-)-malyngolide (IV), through reaction of I with MeOCH(OH)CO2Me to give the intermediate V is also reported.

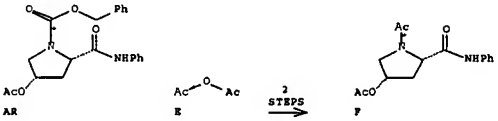
RX(2) OF 205 ...D + E ===> F...



D E F

RX(2) RCT D 77937-78-1, E 108-24-7
PRO F 77937-79-2
CAT 110-86-1 Pyridine

RX(59) OF 205 COMPOSED OF RX(16), RX(2)
RX(59) AR + E ===> F



AR E F

RX(16) RCT AR 77937-77-0
PRO D 77937-78-1

RX(2) RCT D 77937-78-1, E 108-24-7
PRO F 77937-79-2
CAT 110-86-1 Pyridine

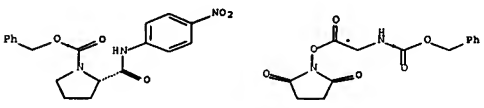
L12 ANSWER 18 OF 18 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 88:7373 CASREACT Full-text
TITLE: Dipeptide derivatives and method for measuring enzyme activity using these derivatives
INVENTOR(S): Nagatsu, Toshiharu; Sakakibara, Shumpei
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2649171	A1	19770518	DE 1976-2649171	19761028
JP 52055593	A	19770507	JP 1975-130809	19751030
JP 56020839	B	19810515		

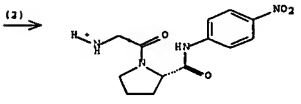
US 4119620	A	19781010	US 1976-733343	19761018
SE 7612064	A	19770501	SE 1976-12064	19761029
NL 7612030	A	19770503	NL 1976-12030	19761029
FR 2329646	A1	19770527	FR 1976-32830	19761029
FR 2329646	B1	19810710		
GB 1518207	A	19780719	GB 1976-45200	19761029
CA 1080216	A1	19800624	CA 1976-264754	19761029
SU 786853	A3	19801207	SU 1976-2415363	19761029
US 4191808	A	19800304	US 1978-897043	19780417
PRIORITY APPLN. INFO.:			JP 1975-130809	19751030
			US 1976-733343	19761018

OTHER SOURCE(S): MARPAT 88:7373
AB H-X-Pro-NHC6H4R-p (I; X = Gly, Ala, Asp, Glu, Lys, Arg; R = NO2; X = Gly, R = N:NPh) and their HCl or tosylate salts were prepared as enzyme substrates for the diagnostic determination of enzymic activities in various diseases. Thus, Z-Pr-OH (Z = PhCH2O2C) was amidated with p-nitroaniline by P(O)Cl3 in THP to give the anilide which was Z-deblocked with HBr/HOAc and coupled to Z-Gly-OSu (Su = succinimido) to give Z-Gly-Pro-NHC6H4NO2-p. The latter was Z-deblocked with HBr/HOAc to give I (X = Gly, R = NO2) (II) which was treated with p-MeC6H4SO3H to give II tosylate (III). III was used as a substrate for the determination of the enzymic activity of human serum by the photometric determination of the resulting p-nitroaniline. The enzymic activity of the serum from patients suffering from various diseases (e.g., hepatitis) was measured with II.

RX(2) OF 3 ...C + D ===> E



C D



E

RX(2) RCT C 21027-63-4, D 2899-60-7
PRO E 60189-43-7

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 273.09 403.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -15.33 -16.06

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 25, 2007 (20070525/UP).

=>
=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.78 404.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE 0.00 -16.06

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STRUCTURE FILE UPDATES: 28 MAY 2007 HIGHEST RN 935999-19-2
DICTIONARY FILE UPDATES: 28 MAY 2007 HIGHEST RN 935999-19-2

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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http://www.cas.org/support/stngen/stndoc/properties.html

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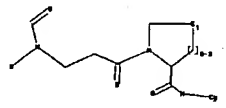
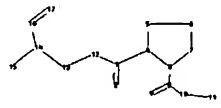
Uploading C:\Program Files\Stnexp\Queries\10.561754\formula VII.str





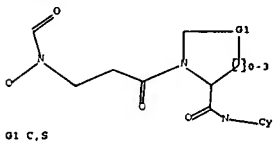
chain nodes :
1 2 8 9 10 11 14 15 16 17
ring nodes :
3 4 5 6 7
ring/chain nodes :
12 13
chain bonds :
1-4 1-2 1-12 3-8 8-9 8-10 10-11 12-13 13-14 14-15 14-16 16-17
ring bonds :
3-4 3-7 4-5 5-6 6-7
exact/norm bonds :
1-4 1-2 1-12 3-4 3-7 3-8 4-5 5-6 6-7 8-9 8-10 10-11 12-13 13-14 14-15
14-16 16-17

G1:C,S

Match level :
1:CLASS 2:CLASS 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:CLASS
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L13 STRUCTURE UPLOADED

=> d
L13 HAS NO ANSWERS
L13 STR



G1 C,S

Structure attributes must be viewed using STN Express query preparation.

=> s l13 sss sam
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SAMPLE SCREEN SEARCH COMPLETED - 23 TO ITERATE

100.0% PROCESSED 23 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

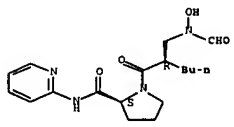
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 173 TO 747
PROJECTED ANSWERS: 4 TO 200

L14 4 SEA SSS SAM L13

=> d scan

L14 4 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-2-pyridinyl-
MF C18 H26 N4 O4

Absolute stereochemistry.



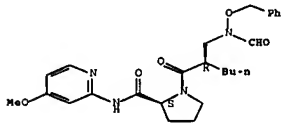
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L14 4 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(4-

methoxy-2-pyridinyl)- (9CI)
MF C26 H34 N4 O5

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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COST IN U.S. DOLLARS SINCE FILE ENTRY 0.45 TOTAL SESSION 404.83

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY 0.00 TOTAL SESSION -16.06

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FILE COVERS 1907 - 30 May 2007 VOL 146 ISS 23
FILE LAST UPDATED: 29 May 2007 (20070529/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l14
L15 4 L14

=> d ibib

L15 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1177562 HCAPLUS Full-text
DOCUMENT NUMBER: 146:92698
TITLE: Peptide deformylase inhibitors as potent antimycobacterial agents
AUTHOR(S): Teo, Jeanette W. P.; Thayalan, Pamela; Beer, David; Yap, Amelia S. L.; Nanjundappa, Mahesh; Ngew, Xinyi; Duraiswamy, Jeyaraj; Liung, Sarah; Dartois, Veronique; Schreiber, Mark; Hasan, Samiul; Cynamon, Michael; Ryder, Neil S.; Yang, Xia; Weidmann, Beat; Bracken, Kathryn; Dick, Thomas; Mukherjee, Kakoli
CORPORATE SOURCE: Novartis Institute for Tropical Diseases, Singapore, 138670, Singapore
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(11), 3665-3673
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib 2-4

L15 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:31167 HCAPLUS Full-text
DOCUMENT NUMBER: 144:121762
TITLE: Method for increasing the susceptibility of peptide deformylase inhibitors by using efflux pump inhibitors
INVENTOR(S): Dean, Charles Richard; Ryder, Neil Stewart
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006002896	A1	20060112	WO 2005-EP7008	20050629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NO, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005259488	A1	20060112	AU 2005-259488	20050629
CA 2569681	A1	20061206	CA 2005-2569681	20050629
EP 1763348	A1	20070321	EP 2005-772146	20050629
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRIORITY APPLN. INFO.:			US 2004-584023P	P 20040630
			WO 2005-EP7008	W 20050629
OTHER SOURCE(S):			MARPAT 144:121762	

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REFERENCE COUNT:          7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15  ANSWER 3 OF 4  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:714250  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:322091
TITLE:                    Role of the AcrAB-TolC efflux pump in determining
                          susceptibility of Haemophilus influenzae to the novel
                          peptide deformylase inhibitor LBM415
AUTHOR(S):                Dean, Charles R.; Narayan, Shubha; Daigle, Denis M.;
                          Dzink-Fox, JoAnn L.; Puyang, Xiaoling; Bracken,
                          Kathryn R.; Dean, Karl E.; Weidmann, Beat; Yuan,
                          Zhengyu; Jain, Rakesh; Ryder, Neil S.
CORPORATE SOURCE:         Novartis Institutes for Biomedical Research, Inc.,
                          Cambridge, MA, 02139, USA
SOURCE:                   Antimicrobial Agents and Chemotherapy (2005), 49(8),
                          3129-3135
                          CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER:                American Society for Microbiology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          35    THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15  ANSWER 4 OF 4  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2002:977804  HCAPLUS  Full-text
DOCUMENT NUMBER:          138:55863
TITLE:                    Preparation of N-formyl-N-hydroxylamino-substituted
                          pyrrolidine derivatives as inhibitors of peptidyl
                          deformylase
INVENTOR(S):              Patel, Dinesh V.; Yuan, Zhengyu; Jain, Rakesh K.;
                          Garcia Alvarez, Salvador; Jacobs, Jeffrey
PATENT ASSIGNEE(S):       Versicor, Inc., USA; Novartis AG
SOURCE:                   PCT Int. Appl., 69 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2002102790        A1    20021227    WO 2002-EP6604         20020614
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU,
             LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG,
             SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     CA 2448526           A1    20021227    CA 2002-2448526        20020614
     AU 2002321062        A1    20030102    AU 2002-321062         20020614
     US 2003045479        A1    20030306    US 2002-171706         20020614
     US 7148242           B2    20061212
     EP 1401828           A1    20040331    EP 2002-754681         20020614
     EP 1401828           B1    20060412
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     HU 2004000208        A2    20040628    HU 2004-208            20020614
     CN 1511152           A     20040707    CN 2002-810596         20020614
     BR 2002010377        A     20040810    BR 2002-10377          20020614
     JP 2005502606        T     20050127    JP 2003-506263         20020614
     NZ 529489            A     20051028    NZ 2002-529489         20020614
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     AT 323081            T     20060415    AT 2002-754681         20020614
     PT 1401828           T     20060831    PT 2002-754681         20020614
     ES 2262824           T3    20061201    ES 2002-2754681        20020614
     ZA 2003008379        A     20040521    ZA 2003-8379           20031028
     IN 2003CN01963       A     20060106    IN 2003-CN1963         20031210
     NO 2003005571        A     20040216    NO 2003-5571           20031212
     HK 1064370           A1    20061020    HK 2004-107013         20040914
PRIORITY APPLN. INFO.:                       US 2001-298419P    P  20010615
                                             US 2002-360313P    P  20020227
                                             WO 2002-EP6604     W  20020614
OTHER SOURCE(S):          MARPAT 138:55863
REFERENCE COUNT:          1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                                9.92     414.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                                0.00     -16.06

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DICTIONARY FILE UPDATES:  28 MAY 2007  HIGHEST RN 935999-19-2

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=> d his

     (FILE 'HOME' ENTERED AT 08:18:24 ON 30 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 08:18:37 ON 30 MAY 2007
L1             STRUCTURE UPLOADED

     FILE 'CASREACT' ENTERED AT 08:19:13 ON 30 MAY 2007
L2             0 S L1 SSS SAM
L3             1 S L1 SSS FULL

     FILE 'REGISTRY' ENTERED AT 08:21:37 ON 30 MAY 2007
L4             STRUCTURE UPLOADED
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     FILE 'CASREACT' ENTERED AT 08:21:56 ON 30 MAY 2007
L5            50 S L4

     FILE 'CASREACT' ENTERED AT 08:24:06 ON 30 MAY 2007
L6            28 S L5 NOT PY>2003

     FILE 'REGISTRY' ENTERED AT 08:28:44 ON 30 MAY 2007
L7             STRUCTURE UPLOADED

     FILE 'CASREACT' ENTERED AT 08:29:13 ON 30 MAY 2007
L8             5 S L7
L9             3 S L8 NOT PY > 2003
L10           46 S L7 SSS FULL
L11           21 S L10 NOT PY >2003
L12           18 S L11 NOT L9

     FILE 'STNGUIDE' ENTERED AT 08:56:10 ON 30 MAY 2007

     FILE 'REGISTRY' ENTERED AT 09:04:03 ON 30 MAY 2007
L13            STRUCTURE UPLOADED
L14            4 S L13 SSS SAM

     FILE 'HCAPLUS' ENTERED AT 09:04:43 ON 30 MAY 2007
L15            4 S L14

     FILE 'REGISTRY' ENTERED AT 09:05:46 ON 30 MAY 2007

=> s l13 sss full
FULL SEARCH INITIATED 09:05:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      444 TO ITERATE

100.0% PROCESSED      444 ITERATIONS                          67 ANSWERS
SEARCH TIME: 00.00.01

L16           67 SEA SSS FUL L13

=> file hcaplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                              172.10     586.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                                0.00     -16.06

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FILE COVERS 1907 - 30 May 2007  VOL 146 ISS 23
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FILE LAST UPDATED: 29 May 2007  (20070529/ED)

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=> s 116
L17           32 L16

=> d ibib abs hitstr tot

L17  ANSWER 1 OF 32  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:269020  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:418201
TITLE:                    Reduced susceptibility of Haemophilus influenzae to
                          the peptide deformylase inhibitor LBM415 can result
                          from target protein overexpression due to amplified
                          chromosomal def gene copy number
AUTHOR(S):                Dean, Charles R.; Narayan, Shubha; Richards, Joel;
                          Daigle, Denis M.; Esterow, Stacy; Leeds, Jennifer A.;
                          Kamp, Heather; Puyang, Xiaoling; Wiedmann, Brigitte;
                          Mueller, Dieter; Voshol, Hans; van Oostrum, Jan; Wall,
                          Daniel; Koehn, James; Dzink-Fox, JoAnn; Ryder, Neil S.
CORPORATE SOURCE:         Infectious Diseases, Novartis Institute for Biomedical
                          Research, Cambridge, MA, 02139, USA
SOURCE:                   Antimicrobial Agents and Chemotherapy (2007), 51(3),
                          1004-1010
                          CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER:                American Society for Microbiology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    Previous genetic anal. of Haemophilus influenzae revealed two mechanisms associated with
      decreased susceptibility to the novel peptide deformylase inhibitor LBM415: AcrAB-TolC-
      mediated efflux and Fmt bypass, resulting from mutations in the pump repressor gene acrR
      and in the fmt gene, resp. The authors have isolated an addnl. mutant, CDS23 (LBM415 MIC
      64 μg/mL vs. 4 μg/mL against the parent strain NB65044) that lacks mutations in the acrR
      or fmt structural genes or in the gene encoding Def, the intracellular target of LBM415.
      Western immunoblot anal., two-dimensional gel electrophoresis, and tryptic digestion
      combined with mass spectrometric identification showed that the Def protein was highly
      overexpressed in the mutant strain.  Consistent with this, real-time reverse
      transcription-PCR revealed a significant increase in def transcript titer.  No mutations
      were found in the region upstream of def that might account for altered expression;
      however, pulsed-field gel electrophoresis suggested that a genetic rearrangement of the
      region containing def had occurred.  Using a combination of PCR, sequencing, and Southern
      blot analyses, it was determined that the def gene had undergone copy number
      amplification, explaining the high level of target protein expression. Inactivation of the
      AcrAB-TolC efflux pump in this mutant increased susceptibility 16-fold, highlighting the
      role of efflux in exacerbating the overall reduced susceptibility resulting from target
      overexpression.
IT    478913-91-6, LBM415
      RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
      BIOL (Biological study)
         (reduced susceptibility of Haemophilus influenzae to peptide
         deformylase inhibitor LBM415 can result from target protein
         overexpression due to amplified chromosomal def gene copy number)
RN    478913-91-6  HCAPLUS
CN    L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-
      oxido-2-pyridinyl)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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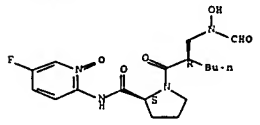


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

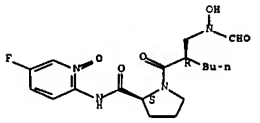
L17 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:148028 HCAPLUS Full-text
DOCUMENT NUMBER: 146:180650
TITLE: Multistep resistance selection and postantibiotic-effect studies of the antipneumococcal activity of LBM415 compared to other agents
AUTHOR(S): Kosowska-Shick, Klaudia; Credito, Kim L.; Pankuch, Glenn A.; DeWasse, Bonifacio; McGhee, Pamela; Appelbaum, Peter C.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(2), 770-773
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB LBM415 is a peptide deformylase inhibitor active against gram-pos. bacterial species and some gram-neg. species. In multiselection studies, LBM415 had low MICs against all Streptococcus pneumoniae strains tested, regardless of their genotype, and selected resistant clones after 14 to 50 days. MIC increases correlated with changes mostly in the 70GXGXAAXQ77 motif in peptide deformylase. The postantibiotic effect of LBM415 ranged from 0.3 to 1.4 h.

IT 478913-91-6, LBM415
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(postantibiotic effect of peptide deformylase inhibitor LBM415 against Streptococcus pneumoniae)

RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

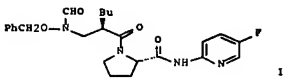
Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1263091 HCAPLUS Full-text
DOCUMENT NUMBER: 146:184267
TITLE: β-Amino amides from β-lactams: application to the formal synthesis of a peptide-deformylase inhibitor
AUTHOR(S): Jiang, Xinglong; Prasad, Kapa; Prashad, Mahavir; Slade, Joel; Repic, Oljan; Blacklock, Thomas J.
CORPORATE SOURCE: Process Research & Development, Novartis Pharmaceuticals Corporation, East Hanover, NJ, 07936, USA
SOURCE: Synlett (2006), (18), 3179-3181
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:184267
GI



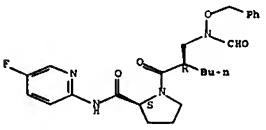
I

AB A facile and a practical synthesis of I, an intermediate for a peptide-deformylase inhibitor, is described using an acid-catalyzed aminolysis of a β-lactam with a pyrrolidine derivative as the key transformation. In addition, simplified conditions for the conversion of a β-hydroxy acid to a β-lactam are reported.

IT 478913-92-7P 771478-83-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(formal synthesis of peptide-deformylase inhibitor via aminolysis of β-lactam)

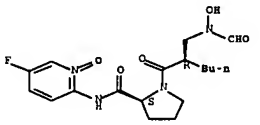
RN 478913-92-7 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 771478-83-2 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)-, magnesium salt (2:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●1/2 Mg

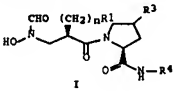
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1250645 HCAPLUS Full-text
DOCUMENT NUMBER: 146:45733
TITLE: Preparation of N-formylhydroxylamine-containing peptides
INVENTOR(S): Bracken, Kathryn Rene; Bushell, Simon; Dean, Karl; Francavilla, Charles; Jain, Rakesh K.; Lee, Kwangho; Seepersaud, Mohindra; Shu, Lei; Sundaram, Arathia; Yuan, Zhengyu
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; Vicuron Pharmaceuticals, Inc
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006127576	A2	20061130	WO 2006-US19688	20060522
WO 2006127576	A3	20070125		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-683655P P 20050523
OTHER SOURCE(S): MARPAT 146:45733
GI



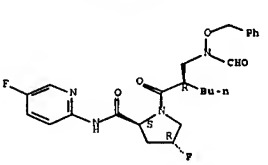
I

AB The invention relates to novel N-formyl hydroxylamine compds. I (R1 is H, alkyl, heteroalkyl, heterocycloalkyl, aryl, or heteroaryl; R3 is H, halo, or alkoxy; R4 is aryl or heteroaryl; n is 0-3) or their salts or prodrugs that inhibit peptidyl deformylase (PDF), an enzyme present in prokaryotes, and are useful as antimicrobials and antibiotics. Examples describe syntheses of title compds. and intermediates, e.g., for the preparation of I (n = 1, R1 = cyclopentyl, R3 = H, R4 = 5-fluoro-N-oxido-2-pyridyl). Compds. of the invention were assayed for inhibition of PDF and for antimicrobial activity (e.g., min. inhibitory concns. .apprx. 0.25-32 μg/mL against H. influenza).

IT 915280-68-1P 915280-69-2P 915280-72-7P
915280-75-0P 915280-77-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-formylhydroxylamine-containing peptides as inhibitors of peptidyl deformylase)

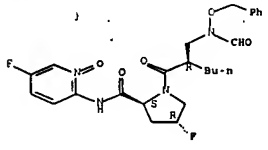
RN 915280-68-1 HCAPLUS
CN 2-Pyrrolidinecarboxamide, 4-fluoro-N-(5-fluoro-2-pyridinyl)-1-[(2R)-2-[[formyl(phenylmethoxy)amino]methyl]-1-oxohexyl]-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.



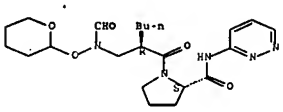
RN 915280-69-2 HCAPLUS
CN 2-Pyrrolidinecarboxamide, 4-fluoro-N-(5-fluoro-1-oxido-2-pyridinyl)-1-[(2R)-2-[[formyl(phenylmethoxy)amino]methyl]-1-oxohexyl]-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.



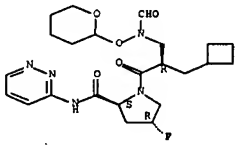
RN 915280-72-7 HCAPLUS
CN 2-Pyrrolidinecarboxamide, 1-[(2R)-2-[[formyl[(tetrahydro-2H-pyran-2-yl)oxy]amino]methyl]-1-oxohexyl]-N-3-pyridazinyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



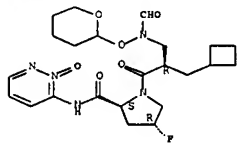
RN 915280-75-0 HCAPLUS
CN 2-Pyrrolidinecarboxamide, 1-[(2R)-3-cyclobutyl-2-[[formyl[(tetrahydro-2H-pyran-2-yl)oxy]amino]methyl]-1-oxopropyl]-4-fluoro-N-3-pyridazinyl-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.



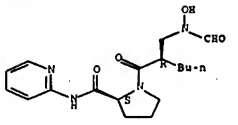
RN 915280-77-2 HCAPLUS
CN 2-Pyrrolidinecarboxamide, 1-[(2R)-3-cyclobutyl-2-[[formyl[(tetrahydro-2H-pyran-2-yl)oxy]amino]methyl]-1-oxopropyl]-4-fluoro-N-(2-oxido-3-pyridazinyl)-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.



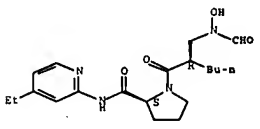
L17 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1177562 HCAPLUS Full-text
DOCUMENT NUMBER: 146:92698
TITLE: Peptide deformylase inhibitors as potent antimycobacterial agents
AUTHOR(S): Teo, Jeanette W. P.; Thayalan, Pamela; Beer, David; Yap, Amelia S. L.; Nanjundappa, Mahesh; Ngew, Xinyi; Duraiswamy, Jeyaraj; Liung, Sarah; Dartois, Veronique; Schreiber, Mark; Hasan, Samiul; Cynamon, Michael; Ryder, Neil S.; Yang, Xia; Weidmann, Beat; Bracken, Kathryn; Dick, Thomas; Mukherjee, Kakoli
CORPORATE SOURCE: Novartis Institute for Tropical Diseases, Singapore, 138670, Singapore
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(11), 3665-3673
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptide deformylase (PDF) catalyzes the hydrolytic removal of the N-terminal formyl group from nascent proteins. This is an essential step in bacterial protein synthesis, making PDF an attractive target for antibacterial drug development. Essentiality of the def gene, encoding PDF from Mycobacterium tuberculosis, was demonstrated through genetic knockout expts. with Mycobacterium bovis BCG. PDF from M. tuberculosis strain H37Rv was cloned, expressed, and purified as an N-terminal histidine-tagged recombinant protein in Escherichia coli. A novel class of PDF inhibitors (PDF-I), the N-alkyl urea hydroxamic acids, were synthesized and evaluated for their activities against the M. tuberculosis PDF enzyme as well as their antimycobacterial effects. Several compds. from the new class had 50% inhibitory concentration (IC50) values of <100 nM. Some of the PDF-I displayed antibacterial activity against M. tuberculosis, including MDR strains with MIC90 values of <1 μM. Pharmacokinetic studies of potential leads showed that the compds. were orally bioavailable. Spontaneous resistance towards these inhibitors arose at a frequency of ≤5×10-7 in M. bovis BCG. DNA sequence anal. of several spontaneous PDF-I-resistant mutants revealed that half of the mutants had acquired point mutations in their formyl methyltransferase gene (fmt), which formylated Met-tRNA. The results from this study validate M. tuberculosis PDF as a drug target and suggest that this class of compds. have the potential to be developed as novel antimycobacterial agents.
IT 478912-45-7, LBK-611
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDF-611; peptide deformylase inhibitors as antimycobacterial agents)
RN 478912-45-7 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-2-pyridinyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 478912-97-9, PDF 709
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide deformylase inhibitors as antimycobacterial agents)
RN 478912-97-9 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-ethyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

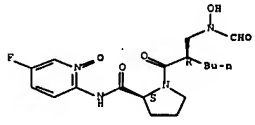


REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:681821 HCAPLUS Full-text
DOCUMENT NUMBER: 145:184160
TITLE: Activity of LBM415 compared to those of 11 other agents against Haemophilus species
AUTHOR(S): Bogdanovich, Tatisna; Smith, Kathy A.; Clark, Catherine; Pankuch, Glenn A.; Lin, Gengrong; McGhee, Pamela; Dewasse, Bonifacio; Appalbaum, Peter C.
CORPORATE SOURCE: Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(7), 2323-2329
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When tested against 254 Haemophilus influenzae strains, LBM415, a peptide deformylase inhibitor, gave MIC50 and MIC90 values of 2.0 μg/mL and 8.0 μg/mL, resp. The MICs were independent of β-lactam or quinolone susceptibility and the presence or absence of macrolide efflux or ribosomal protein mutations. The MICs of LBM415 against 23 H. parainfluenzae strains were similar to those against H. influenzae. In contrast, erythromycin, azithromycin, and clarithromycin gave unimodal MIC distributions, and apart from β-lactamase-neg., ampicillin-resistant strains, all strains were susceptible to the β-lactams tested. Apart from selected quinolone-resistant strains, all strains were susceptible to ciprofloxacin, levofloxacin, gatifloxacin, moxifloxacin, and gemifloxacin. Resistance to trimathoprim-sulfamethoxazole was common. The potencies of all drugs

against 23 H. parainfluenzae strains were similar to those against H. influenzae. Time-kill studies with 10 Haemophilus strains showed LBM415 to be bactericidal at 2 × the MIC against 8 of 10 strains after 24 h. For comparison, the macrolides and β-lactams were bactericidal against 8 to 10 strains each at 2 × the MIC after 24 h. Quinolones were bactericidal against all 10 strains tested at 2 × the MIC after 24 h. Against six H. influenzae strains, postantibiotic effects for LBM415 lasted between 0.8 and 2.2 h. In multi-step resistance selection studies, LBM415 produced resistant clones in 7 of the 10 strains tested, with MICs ranging from 4 to 64 μg/mL. No mutations in deformylase (def) and formyltransferase (fmt) genes were detected in any of the LBM415-resistant mutants.
IT 478913-91-6, LBM415
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activity of LBM415 compared to other agents against Haemophilus species)
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

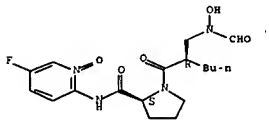
L17 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:446747 HCAPLUS Full-text
DOCUMENT NUMBER: 144:484488
TITLE: Proteomic study of peptide deformylase inhibition in Streptococcus pneumoniae and Staphylococcus aureus
AUTHOR(S): Wang, Wen; White, Richard; Yuan, Zhengyu
CORPORATE SOURCE: Vicuron Pharmaceuticals, Fremont, CA, 94555, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(5), 1656-1663
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptide deformylase (PDF) is an essential enzyme in both gram-neg. and gram-pos. bacteria. It hydrolyzes formylated N-terminal peptides to generate free N-terminal peptides during the process of protein maturation. Inhibition of this enzyme results in cessation of bacterial growth. We have examined the effect of a potent PDF inhibitor, LBM-415 (also known as VIC-104959), on the proteomes of Staphylococcus aureus and Streptococcus pneumoniae using two-dimensional electrophoresis. Both S. aureus and S. pneumoniae showed accumulation of many N-terminal formylated peptides/proteins upon PDF inhibition. In S. pneumoniae, formylated peptide/protein accumulation was time dependent. Following inhibition, subsequent removal of the inhibitor resulted in deformylation of formylated peptides/proteins; this recovery process was also time dependent. If instead the inhibited cells were maintained in the presence of sub-MIC levels of the PDF inhibitor, the formylated peptides/proteins remained for a much longer time, which correlated with a prolonged postantibiotic effect in vitro. These observations may have broader implications for the application of this class of antibiotics in vivo.
IT 478913-91-6, LBM-415

RL: BSU (Biological study, unclassified); BIOL (Biological study) (PDF inhibitor; proteomic study of peptide deformylase inhibition in Streptococcus pneumoniae and Staphylococcus aureus)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:332553 HCAPLUS Full-text

DOCUMENT NUMBER: 145:79591

TITLE: Antimicrobial activity of a novel peptide deformylase inhibitor, LBM415, tested against respiratory tract and cutaneous infection pathogens: a global surveillance report (2003-2004)

AUTHOR(S): Watters, Amy A.; Jones, Ronald N.; Leeds, Jennifer A.; Denys, Gerald; Sader, Helio S.; Fritsche, Thomas R.

CORPORATE SOURCE: JMI Laboratories, North Liberty, IA, 52317, USA

SOURCE: Journal of Antimicrobial Chemotherapy (2006), 57(5), 914-923
CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To evaluate the spectrum of activity and potency of LBM415, the 1st of the peptide deformylase inhibitor (PDFI) class to be developed for treatment of community-acquired respiratory tract infections and uncomplicated skin and soft tissue infections (uSSTI), against a large, contemporary international collection of targeted pathogens collected during 2003-2004. A total of 21 636 isolates were tested by reference broth microdilution methods as part of a longitudinal international antimicrobial resistance surveillance study. Characteristics of the organism collection included resistance to oxacillin among 35.0% of Staphylococcus aureus and 76.0% of coagulase-neg. staphylococci (CoNS); resistance to penicillin (MIC ≥ 2 mg/L) among 18.0% of Streptococcus pneumoniae; vancomycin resistance among 20.0% of Enterococcus spp. and ampicillin resistance among 22.0% of Haemophilus influenzae. LBM415 displayed potent activity against staphylococci, streptococci, Enterococcus faecium and Moraxella catarrhalis, with ≥99.0% of strains being inhibited at ≤4 mg/L; 97.0% of Enterococcus fecalis isolates and 92.0% of H. influenzae isolates were also inhibited at this concentration Seventy-seven % of Burkholderia cepacia and 82.0% of Stenotrophomonas maltophilia were inhibited at ≤8 mg/L. No differences in LBM415 activity against S. aureus, CoNS, S. pneumoniae, Enterococcus spp. and H. influenzae were detected for subsets susceptible or resistant to antimicrobials such as oxacillin, penicillin, ampicillin, macrolides, vancomycin and fluoroquinolones. While regional differences were apparent with some comparator agents, sensitivity to LBM415 did not vary significantly among strains from the various geog. areas sampled. One isolate of S. aureus displayed high-level resistance to LBM415 owing to multiple sequence changes in resistance phenotype genes (defB and fmt), despite the absence of the compound

in clin. practice. This isolate remained susceptible to all other antimicrobials tested except for penicillin. With few differences detected among strains from various geog. regions, the 1st PDFI class agent to enter clin. development has consistently demonstrated a broad spectrum of activity against commonly isolated pathogens associated with uncomplicated respiratory and cutaneous infections. These compds. represent a significant therapeutic advance owing to their novel mechanism of action and antibacterial spectrum, including activity against resistant organisms, should pharmacokinetic and pharmacodynamic parameters support their continued development. Given the detection of a pre-existing PDFI-resistant isolate of S. aureus as demonstrated here, surveillance for resistance among the PDFI-targeted pathogens following introduction of this class of agent into clin. usage will be an important component of future studies.

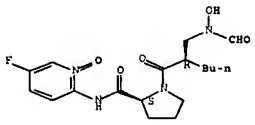
IT 478913-91-6, LBM415

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of peptide deformylase inhibitor LBM415 against respiratory tract and cutaneous infection pathogens)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:206088 HCAPLUS Full-text

DOCUMENT NUMBER: 144:424953

TITLE: Natural products - the future scaffolds for novel antibiotics?

AUTHOR(S): Butler, Mark S.; Buss, Antony D.

CORPORATE SOURCE: MerLion Pharmaceuticals, Singapore, 117528, Singapore

SOURCE: Biochemical Pharmacology (2006), 71(7), 919-929
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Natural products have played a pivotal role in antibiotic drug discovery with most antibacterial drugs being derived from a natural product or natural product lead. However, the rapid onset of resistance to most antibacterial drugs diminishes their effectiveness considerably and necessitates a constant supply of new antibiotics for effective treatment of infections. The natural product templates of actinonin, pleuromutilin, ramoplanin and tiacumicin B, which are compds. undergoing clin. evaluation, represent templates not found in currently marketed antibacterial drugs. In addition, the new templates present in the recently discovered lead antibacterials arylomycin, GE23077, mannopeptimycin, muraymycin/caprazamycin, nocathiacin and ECO-0501, are discussed. Despite extensive efforts to identify antibiotic leads from mol. targets, only the peptide deformylase inhibitor LBM-415 is currently in clin. trials. It is proposed that new antibacterial assays which combine cell-based screening with mol. targets could offer better prospects for lead discovery.

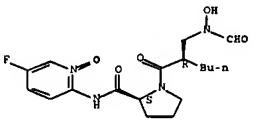
IT 478913-91-6, LBM 415

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(natural products)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:31167 HCAPLUS Full-text

DOCUMENT NUMBER: 144:121762

TITLE: Method for increasing the susceptibility of peptide deformylase inhibitors by using efflux pump inhibitors

INVENTOR(S): Dean, Charles Richard; Ryder, Neil Stewart

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH

SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006002896	A1	20060112	WO 2005-EP7008	20050629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005259488	A1	20060112	AU 2005-259488	20050629
CA 2569681	A1	20061206	CA 2005-2569681	20050629
EP 1763348	A1	20070321	EP 2005-772146	20050629
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-584023P P 20040630
WO 2005-EP7008 W 20050629

OTHER SOURCE(S): MARPAT 144:121762

AB The invention provides methods and compns. for increasing the susceptibility of peptide deformylase inhibitors against Gram-neg. organisms by using efflux pump inhibitors. Related methods for the treatment of Gram-neg. bacterial infections are also provided.

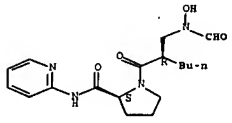
IT 478912-45-7, LBK 611 478913-91-6

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for increasing the susceptibility of peptide deformylase inhibitors by using efflux pump inhibitors)

RN 478912-45-7 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-2-pyridinyl- (CA INDEX NAME)

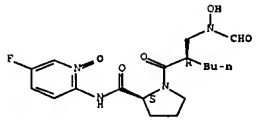
Absolute stereochemistry.



RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1093778 HCAPLUS Full-text

DOCUMENT NUMBER: 143:359507

TITLE: Evaluation of LBM415 (NVP PDF-713), a novel peptide deformylase inhibitor, for treatment of experimental Mycoplasma pneumoniae pneumonia

AUTHOR(S): Fonseca-Aten, Monica; Salvatore, Christine M.; Mejias, Asuncion; Rios, Ana M.; Chavez-Bueno, Susana; Katz, Kathy; Gomez, Ana M.; McCracken, George H., Jr.; Hardy, R. Doug

CORPORATE SOURCE: Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX, 75390-9063, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(10), 4128-4136

CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

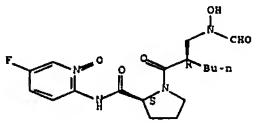
AB Mycoplasma pneumoniae is a major cause of community-acquired pneumonia. We evaluated the efficacy of LBM415, a novel peptide deformylase inhibitor antimicrobial agent, for the treatment of M. pneumoniae pneumonia in a mouse model. Eight-week-old BALB/c mice were intranasally inoculated once with 10⁷ CFU of M. pneumoniae. Groups of mice were treated with LBM415 (50 mg/kg of body weight) or placebo s.c. daily for 13 days, starting 24 h after inoculation. Groups of mice were evaluated at the baseline; at days of treatment 1, 3, 6, and 13; and at 7 days after treatment. The MIC of LBM415 against M. pneumoniae was <0.005 μg/mL. LBM415-treated mice had significantly lower bronchoalveolar lavage fluid M. pneumoniae concns. than placebo-treated mice on days 6 and 13 of treatment. Compared with placebo treatment, therapy with LBM415 significantly decreased lung histopathol. scores at days 3, 6, and 13 of treatment and at 7 days after treatment. Airway obstruction was significantly lower in LBM415-treated mice than in placebo-treated mice on days 1, 3, and 6 of treatment and after 7 days of therapy, while airway hyperresponsiveness was significantly lower only on day 3 of therapy. The bronchoalveolar lavage fluid concns. of tumor necrosis factor alpha, gamma interferon (IFN-γ), interleukin-6 (IL-6), IL-12, KC (functional IL-8), monocyte chemotactic protein 1, macrophage inflammatory protein 1α, monokine induced by IFN-γ, and IFN-inducible protein 10 were significantly reduced in LBM415-treated mice compared with the levels in placebo-treated mice. There were no differences in the bronchoalveolar lavage fluid concns. of granulocyte-macrophage colony-stimulating factor, IL-1β, IL-2, IL-4, IL-5, and IL-10 between the two groups of mice. LBM415 therapy had beneficial microbiol., histol., respiratory, and immunol. effects on acute murine M. pneumoniae pneumonia.

IT 478913-91-6, LBM415
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LBM415 (NVP PDF-713), a novel peptide deformylase inhibitor, for treatment of exptl. Mycoplasma pneumoniae pneumonia)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:714250 HCAPLUS Full-text
DOCUMENT NUMBER: 143:322091
TITLE: Role of the AcrAB-TolC efflux pump in determining susceptibility of Haemophilus influenzae to the novel peptide deformylase inhibitor LBM415
AUTHOR(S): Dean, Charles R.; Narayan, Shubha; Daigle, Denis M.; Dzink-Fox, JoAnn L.; Puyang, Xiaoling; Bracken, Kathryn R.; Dean, Karl E.; Weidmann, Beat; Yuan, Zhengyu; Jain, Rakesh; Ryder, Neil S.

CORPORATE SOURCE: Novartis Institutes for Biomedical Research, Inc., Cambridge, MA, 02139, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(8), 3129-3135
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

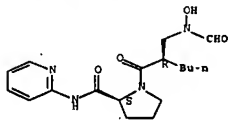
AB Haemophilus influenzae isolates vary widely in their susceptibilities to the peptide deformylase inhibitor LBM415 (MIC range, 0.06 to 32 μg/mL); however, on average, they are less susceptible than gram-pos. organisms, such as Staphylococcus aureus and Streptococcus pneumoniae. Insertional inactivation of the H. influenzae acrB or tolC gene in strain NB65044 (Rd strain KW20) increased susceptibility to LBM415, confirming a role for the AcrAB-TolC pump in determining resistance. Consistent with this, sequencing of a PCR fragment generated with primers flanking the acrRA region from an LBM415-hypersusceptible H. influenzae clin. isolate revealed a genetic deletion of acrA. Inactivation of acrB or tolC in several clin. isolates with atypically reduced susceptibility to LBM415 (MIC of 16 μg/mL or greater) significantly increased susceptibility, confirming that the pump is also a determinant of decreased susceptibility in these clin. isolates. Examination of acrR, encoding the putative repressor of pump gene expression, from several of these strains revealed mutations introducing frameshifts, stop codons, and amino acid changes relative to the published sequence, suggesting that loss of pump repression leads to decreased susceptibility. Supporting this, NB65044 acrR mutants selected by exposure to LBM415 at 8 μg/mL had susceptibilities to LBM415 and other pump substrates comparable to the least sensitive clin. isolates and showed increased expression of pump genes.

IT 478912-45-7, LBK 611
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AcrR is repressor of AcrAB expression, and mutations in acrR are related to susceptibility to LBM415)

RN 478912-45-7 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-2-pyridinyl- (CA INDEX NAME)

Absolute stereochemistry.

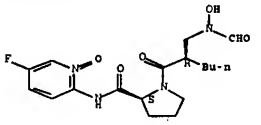


IT 478913-91-6, LBM415
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of AcrAB-TolC efflux pump in determining susceptibility of Haemophilus influenzae to novel peptide deformylase inhibitor LBM415 and structurally related LBK611)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:602838 HCAPLUS Full-text
DOCUMENT NUMBER: 143:169417
TITLE: Evaluation of the in vitro activity of NVP-LMB415 against clinical anaerobic isolates with emphasis on the Bacteroides fragilis group
AUTHOR(S): Snydman, David R.; Jacobus, Nilda V.; McDermott, Laura A.
CORPORATE SOURCE: Tufts-New England Medical Center, Boston, MA, 02111, USA
SOURCE: Journal of Antimicrobial Chemotherapy (2005), 55(6), 1024-1028
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

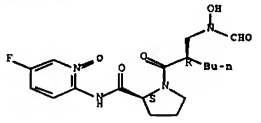
AB Objectives: To compare the in vitro activity of NVP-LMB415 (formerly referred to as NVP-PDF 713) with that of other agents with anti-anaerobe activity against clin. anaerobic isolates, with emphasis on the Bacteroides fragilis group. The MICs for 405 B. fragilis group and 102 Gram-pos. anaerobic isolates were determined using NCCLS-recommended procedures. The activity of NVP-LMB415 was compared with that of cefoxitin, clindamycin, imipenem, gemifloxacin, linezolid, moxifloxacin and tigecycline. Vancomycin was included in the evaluation of the Gram-pos. organisms. NVP-LMB415 showed excellent in vitro activity against all the species of the B. fragilis group isolates (MIC range ≤ 0.03-0.5 mg/L and MIC90 0.5 mg/L). NVP-LMB415 was active against B. fragilis group strains resistant to β-lactams, quinolones or clindamycin, and the MICs were much lower than those of newer agents such as linezolid, tigecycline and gemifloxacin. The MICs of NVP-LMB415 (≥ 4 mg/L) for Clostridium species were higher than the MICs for other anaerobes. Given the frequency of isolation of anaerobic bacteria and their increasing resistance to all classes of antibiotics, NVP-LMB415 is an ideal agent for potential use against mixed infections caused by resistant anaerobic pathogens such as of B. fragilis and Gram-pos. aerobic strains such as methicillin-resistant staphylococci, streptococci and enterococci.

IT 478913-91-6, NVP-PDF 713
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Evaluation of the in vitro activity of NVP-LMB415 against clin. anaerobic isolates with emphasis on the Bacteroides fragilis group)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:553883 HCAPLUS Full-text
DOCUMENT NUMBER: 143:221622
TITLE: Bacterial peptide deformylase inhibitors: A new class of antibacterial agents
AUTHOR(S): Jain, R.; Chen, D.; White, R. J.; Patel, D. V.; Yuan, Z.
CORPORATE SOURCE: Vicuron Pharmaceuticals, Fremont, CA, 94555, USA
SOURCE: Current Medicinal Chemistry (2005), 12(14), 1607-1621
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

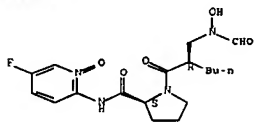
AB A review. Peptide deformylase (PDF) is a prokaryotic metalloenzyme that is essential for bacterial growth but is not required by mammalian cells. Thus, it represents a selective and promising target for the development of new antibacterial agents. Since deformylase inhibitors have yet to be used clin. as antibacterial drugs, compds. targeting this enzyme should avoid cross-resistance with currently used antibacterial agents. The PDF enzyme is a ferrous ion-containing metallohydrolase, but a nickel-containing surrogate is routinely used in the laboratory for testing inhibitors due to its better stability. Enzymes from several bacterial species have been cloned and both their three-dimensional structures and co-crystal structures with bound inhibitor have been determined As a metallo enzyme, PDF lends itself to the well-precedented mechanism-based rational drug design approach. Using structural and mechanistic information together with high throughput screening, several types of potent PDF inhibitors have been identified. PDF inhibitors identified to date share a common structural feature of a "chelator + peptidomimetic" scaffold. Although compds. with many different chelators inhibit the cell free enzyme, only compds. containing hydroxamic acid or N-formyl hydroxylamine exhibit appreciable antibacterial activity. Several lead inhibitors have demonstrated in vivo efficacy and an excellent safety profile. Two PDF inhibitors, VIC-104959 (LBM415) and BB-83698, have progressed to Phase I clin. trials. In this review, different PDF inhibitors are compared and their biol. activities are discussed. Structure-activity relationships have been established and the implications of this work in the design of future PDF inhibitors are considered.

IT 478913-91-6, VIC 104959
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bacterial peptide deformylase inhibitors as a new class of antibacterial agents)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:494346 HCAPLUS Full-text
DOCUMENT NUMBER: 143:149764
TITLE: Comparative in vitro activities of investigational peptide deformylase inhibitor NVP LBM-415 and other agents against human mycoplasmas and ureaplasmas
AUTHOR(S): Waites, Ken B.; Reddy, Nipun B.; Crabb, Donna M.; Duffy, Lynn B.
CORPORATE SOURCE: Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, 35249, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(6), 2541-2542
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

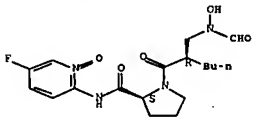
AB Peptide deformylase inhibitor LBM-415 and seven other drugs were tested against Mycoplasma pneumoniae (100 isolates), Mycoplasma hominis (20 isolates), Mycoplasma fermentans (10 isolates), and Ureaplasma species (50 isolates). LBM-415 was active against M. pneumoniae (MICs, ≤0.008 µg/mL). It showed no activity against M. hominis and M. fermentans and modest activity against Ureaplasma spp.

IT 478913-91-6, LBM-415
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(comparative in vitro activities of investigational peptide deformylase inhibitor NVP LBM-415 and other agents against human mycoplasmas and ureaplasmas)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:494343 HCAPLUS Full-text
DOCUMENT NUMBER: 143:149763
TITLE: In vitro and intracellular activities of LBM415 (NVP PDF-713) against Legionella pneumophila
AUTHOR(S): Edelstein, Paul H.; Hu, Baofeng; Edelstein, Martha A. C.
CORPORATE SOURCE: Departments of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-4283, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(6), 2533-2535
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

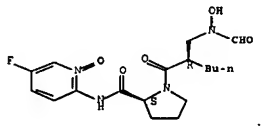
AB LBM415 activity against extracellular and intracellular L. pneumophila was studied. The LBM415 MIC50 for 20 Legionella sp. strains was 4 µg/mL, vs. 0.06, 0.25, and ≤ 0.03 µg/mL for azithromycin, erythromycin, and levofloxacin, resp. LBM415 (0.5 and 16 µg/mL) reversibly prevented intracellular growth of 2 L. pneumophila strains and was less active than erythromycin.

IT 478913-91-6, LBM415
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro and intracellular activities of LBM415 against Legionella pneumophila)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:375159 HCAPLUS Full-text
DOCUMENT NUMBER: 142:475186
TITLE: LBM-415: Antibacterial peptide deformylase inhibitor
AUTHOR(S): McIntyre, J. A.; Castaner, J.; Martin, L.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2005), 30(1), 23-28
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Resistance among bacterial pathogens has necessitated the search for novel targets in antimicrobial research. The peptide deformylase inhibitors are a novel and unique class of antimicrobial agents in development for the treatment of respiratory tract and skin infections. LBM-415 is the first such compound to enter clin. development. Its

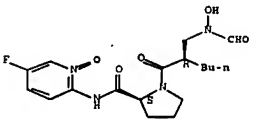
activity has been widely evaluated in preclin. studies against multiple pathogens, including drug-resistant strains. In vitro studies using recent clin. isolates have demonstrated potent activity against streptococcal and staphylococcal strains responsible for community-acquired respiratory tract infections and skin infections. LBM-415 is also active against medically important groups of drug-resistant pathogens, including methicillin-resistant Staphylococcus aureus (MRSA), penicillin-resistant Streptococcus pneumoniae, vancomycin-resistant enterococci and clarithromycin-resistant Helicobacter pylori. The efficacy of LBM-415 has been demonstrated in mouse models of infection, where it was active against Mycoplasma pneumoniae-induced pneumonia, and had comparable efficacy to linezolid and vancomycin against systemic MRSA and methicillin-susceptible S. aureus (MSSA). Pharmacokinetic studies, including single- and multiple-dose studies in humans, demonstrated linear kinetics, with rapid absorption of LBM-415 and no evidence of accumulation. The compound is advancing to phase II/III clin. trials.

IT 478913-91-6, LBM 415
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide deformylase inhibitor LBM-415 was active against drug-resistant pathogens, was effective in mouse models of infection and had linear kinetics with rapid absorption and no evidence of accumulation in human)

RN 478913-91-6 HCAPLUS

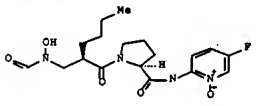
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:325026 HCAPLUS Full-text
DOCUMENT NUMBER: 143:22918
TITLE: Comparative antimicrobial characterization of LBM415 (NVP PDF-713), a new peptide deformylase inhibitor of clinical importance
AUTHOR(S): Fritsche, Thomas R.; Sader, Helio S.; Cleeland, Roy; Jones, Ronald N.
CORPORATE SOURCE: The JONES Group/JMI Laboratories, North Liberty, IA, 52317, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(4), 1468-1476
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

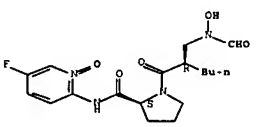
AB LBM415 (NVP PDF-713) (I) is the first member of the peptide deformylase (PDF) inhibitor class being developed for clin. trials as a parenteral and oral agent for treatment of community-acquired respiratory tract disease and serious infections caused by antimicrobial-resistant gram-pos. cocci. In this study, susceptibility testing results from 1,306 recent clin. isolates selected to overrepresent resistance trends among the species were summarized. All staphylococci (153 strains; MIC at which 90% of isolates were inhibited [MIC90], 2 µg/mL), Streptococcus pneumoniae (170 strains; MIC90, 1 µg/mL), other streptococci (150 strains; MIC90, 1 µg/mL), enterococci (104 strains; MIC90, 4 µg/mL), Moraxella catarrhalis (103 strains; MIC90, 0.5 µg/mL), and Legionella pneumophila (50 strains; MIC90, 0.12 µg/mL) were inhibited at ≤8 µg of LBM415/mL, as were 97% of Haemophilus influenzae isolates (300 strains; MIC90, 4 to 8 µg/mL). Among other bacterial groups, 100% of gram-pos. and -neg. anaerobes, including 22 Bacteroides spp. strains (31 strains total; MIC90, 1 µg/mL), were inhibited by ≤4 µg/mL, whereas Enterobacteriaceae (112 strains) and most nonfermentative bacilli (107 strains) were not inhibited at readily achievable concns. The compound was found to have a dominantly bacteriostatic action, and spontaneous single-step mutational rates occurred at low levels (10-6 to <10-8). Drug interaction studies failed to identify any class-specific synergistic interactions, nor were antagonistic interactions observed. Variations in broth and agar MIC test conditions demonstrated that, whereas the agar-based method trended towards a 1-log2 dilution-higher MIC than the broth method and was inoculum dependent, other variations in incubation environment, medium supplements, pH, or calcium concentration had little influence on LBM415 MIC results. Use of the efflux inhibitor phe-arg-β-naphthylamide showed an average of 1 log2 dilution decrease in H. influenzae MICs, demonstrating the contribution of efflux pumps in influencing susceptibility to PDF inhibitors. The in vitro activity of LBM415 against targeted bacterial species, including resistant subsets, and other laboratory characteristics of this novel compound demonstrate the potential of PDF inhibitors as a new class of antimicrobial agents.

IT 478913-91-6, LBM415
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(comparative antibacterial characterization of LBM415 as new peptide deformylase inhibitor of clin. importance)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

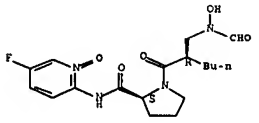
Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:109471 HCAPLUS Full-text
DOCUMENT NUMBER: 142:459965
TITLE: Antimicrobial activity of LBM415 (NVP PDF-713) tested against pathogenic Neisseria spp. (Neisseria gonorrhoeae and Neisseria meningitidis)
AUTHOR(S): Jones, Ronald N.; Sader, Helio S.; Fritsche, Thomas R.
CORPORATE SOURCE: The JONES Group, JMI Laboratories Inc., North Liberty, IA, 52317, USA
SOURCE: Diagnostic Microbiology and Infectious Disease (2005), 51(2), 139-141
CODEN: DMIDDZ; ISSN: 0732-8893
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB LBM415 (NVP PDF-713), a novel peptide deformylase inhibitor, was tested by reference methods against 2 collections of pathogenic Neisseria, N. gonorrhoeae (157 strains) and N. meningitidis (100 strains). The collection included strains resistant to penicillin, tetracycline, and fluoroquinolones and were also tested against ceftriaxone, ciprofloxacin, penicillin, and tetracycline. The 50% and 90% min. inhibitory concentration values for LBM415 were 1 and 2 μg/mL, and 4 and 8 μg/mL for N. meningitidis and N. gonorrhoeae, resp. All comparison agents were more active than this peptide deformylase inhibitor against this genus.
IT 478913-91-6, LBM 415
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimicrobial activity of deformylase inhibitor LBM415 (NVP PDF-713) against pathogenic Neisseria gonorrhoeae and N. meningitidis)
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

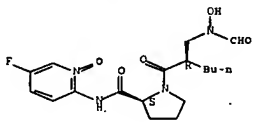


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:88905 HCAPLUS Full-text
DOCUMENT NUMBER: 143:93836
TITLE: Activity of a peptide deformylase inhibitor LBM415 (NVP PDF-713) tested against recent clinical isolates from Japan
AUTHOR(S): Bell, Jan M.; Turnidge, John D.; Inoue, Matsuhisa; Kohno, Shigeru; Hirakata, Yoichi; Ono, Yasuo; Jones, Ronald N.
CORPORATE SOURCE: Women's and Children's Hospital, Adelaide, Australia
SOURCE: Journal of Antimicrobial Chemotherapy (2005), 55(2),

276-278
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potency of LBM415, a new peptide deformylase (PDF) inhibitor, against key Gram-pos. pathogens, as well as Haemophilus influenzae, from Japan was assessed. A total of 695 clin. isolates originally collected in Japan included Staphylococcus aureus (n=222), Haemophilus influenzae, Streptococcus pneumoniae (n=122), coagulase-neg. staphylococci (CoNS, n=119), Enterococcus spp. (n=65) and Streptococcus spp. (n=48). Oxacillin-resistant S. aureus had slightly lower LBM415 MIC values than oxacillin-susceptible strains. MIC50 and MIC90 values of LBM415 against oxacillin-resistant S. aureus were 2 log10 dilns. lower than previous findings. CoNS had similar MIC results to S. aureus, although oxacillin-resistant strains appeared to be less susceptible than oxacillin-susceptible strains. All enterococci were inhibited at ≤8 mg/L of LBM415, all S. pneumoniae were inhibited at ≤2 mg/L of the PDF inhibitor, regardless of penicillin or multi-drug resistance. The LBM415 MIC90 for the β-hemolytic streptococci was 0.5 mg/L; all streptococci were inhibited at ≤4 mg/L. These results indicate that LBM415 appears to be an active agent that may be suitable for the treatment of infections, caused by Gram-pos. organisms.
IT 478913-91-6, LBM 415
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activity of peptide deformylase inhibitor LBM415 (NVP PDF-713) tested against recent clin. isolates from Japan)
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

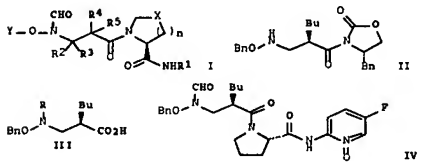
L17 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:14391 HCAPLUS Full-text
DOCUMENT NUMBER: 142:113909
TITLE: Process for preparation of N-[oxidopyridinyl)-L-prolinamide derivatives
INVENTOR(S): Slade, Joel; Vivelo, James Anthony; Chen, Guang-Pei; Bajwa, Joginder Singh; Parker, David John
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000835	A1	20050106	WO 2004-EP6915	20040625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

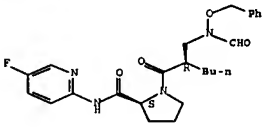
AU 2004251876	A1	20050106	AU 2004-251876		20040625
CA 2530142	A1	20050106	CA 2004-2530142		20040625
EP 1641778	A1	20060405	EP 2004-740324		20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004011921	A	20060815	BR 2004-11921		20040625
CN 1829710	A	20060906	CN 2004-80021438		20040625
US 2007060753	A1	20070315	US 2005-561754		20051221
PRIORITY APPLN. INFO.:			US 2003-482686P	P	20030626
			WO 2004-EP6915	W	20040625

OTHER SOURCE(S): CASREACT 142:113909; MARPAT 142:113909
GI



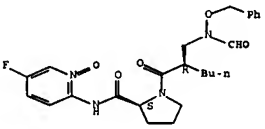
AB A process for the preparation of title compds. of formula I [Y = a OH protecting group; R1 = (hetero)aryl; R2-R5 = independently H or alkyl, or R2R3 and/or R4R5 = cycloalkyl; X = CH2, S, CH(OH), etc.; n = 0-3] is disclosed. For example, contacting II•TsOH with 1N Na2CO3 in EtOAc to move TsOH and oxidation by H2O2 gave III (R = H). Formylation of III with formic acetic anhydride gave III (R = CHO). Reaction of III with HBr salt of N-(5-fluoro-2-pyridinyl)-2-pyrrolidinecarboxamide, followed by oxidation , gave IV. Thus, the present invention provides a process producing the title compound, which are useful to prepare certain antibacterial N-formyl hydroxylamine compds. as peptide deformylase inhibitors.
IT 478913-92-7P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-[oxidopyridinyl) L-prolinamide derivs.)
RN 478913-92-7 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 478913-93-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of N-[oxidopyridinyl) L-prolinamide derivs.)
RN 478913-93-8 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

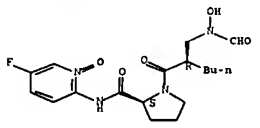


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:915738 HCAPLUS Full-text
DOCUMENT NUMBER: 142:35071
TITLE: Commercial broth microdilution panel validation and reproducibility trials for NVP PDF-713 (LBM 415), a novel inhibitor of bacterial peptide deformylase
AUTHOR(S): Fritsche, T. R.; Moet, G. J.; Jones, R. N.
CORPORATE SOURCE: The JONES Group/JMI Laboratories, North Liberty, IA, USA
SOURCE: Clinical Microbiology and Infection (2004), 10(9), 857-860
CODEN: CMINFM; ISSN: 1198-743X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NVP PDF-713 (LBM 415) is a peptide deformylase inhibitor being progressed into clin. trials. Dry-form broth microdilution panels of NVP PDF-713 were compared to reference MIC panels of 552 recent clin. isolates. Most (99.2%) dry-form MIC results were within ± 1 log2 dilution of the reference panel MICs. Of the bacteria tested, Streptococcus pneumoniae and Haemophilus influenzae showed a bias towards higher and lower MICs, resp. Same-day and between-day reproducibility tests showed that 98.9% and 96.7% of MIC values, resp., were within ± 1 log2 dilution step, thereby demonstrating a high degree of reliability of the dry-form MIC product for clin. studies.

IT 478913-91-6
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimicrobial activity of peptide deformylase inhibitor NVP PDF-713 against respiratory tract pathogens)
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



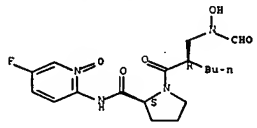
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:857380 HCAPLUS Full-text
DOCUMENT NUMBER: 141:337761
TITLE: Crystalline N-formylhydroxylamine compounds for pharmaceuticals
INVENTOR(S): Mueller, Martin; Liu, Hui; Bajwa, Joginder Singh
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH; Slade, Joel
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087133	A1	20041014	WO 2004-EP3478	20040401
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004226815	A1	20041014	AU 2004-226815	20040401
CA 2520682	A1	20041014	CA 2004-2520682	20040401
EP 1613305	A1	20060111	EP 2004-725014	20040401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009009	A	20060328	BR 2004-9009	20040401
CN 1764450	A	20060426	CN 2004-80007872	20040401
JP 2006522054	T	20060928	JP 2006-504952	20040401
NO 2005005097	A	20051222	NO 2005-5097	20051101

PRIORITY APPLN. INFO.: US 2003-459726P P 20030402
WO 2004-EP3478 A 20040401
OTHER SOURCE(S): MARPAT 141:337761
AB Certain N-formylhydroxylamine compds., such as N-[1-oxo-2-alkyl-3-(N-hydroxyformamido)propyl](carbonylaminoaryl)azacycloalkanes are useful in the treatment of bacterial infections. Disclosed are crystalline salts of such compds. Thus, a capsule contained a N-formylhydroxylamine 200, spray-dried lactose 148, and Mg stearate 2 mg. 1-[2-R- [(formylhydroxylamino)methyl]hexanoyl]pyrrolidone-2S-carboxylic acid-(4-ethylpyridin-2-yl)amide was converted to its calcium salt by reaction with CaCl2 solution in NaOH solution
IT 771478-83-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline N-formylhydroxylamine compds. for pharmaceuticals)
RN 771478-83-2 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)-, magnesium salt (2:1) (9CI) (CA INDEX NAME)

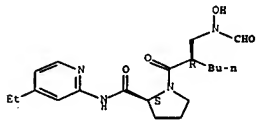
Absolute stereochemistry.



●1/2 Mg

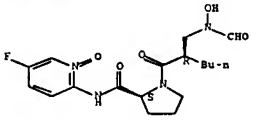
IT 478912-97-9 478913-91-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystalline N-formylhydroxylamine compds. for pharmaceuticals)
RN 478912-97-9 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-ethyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



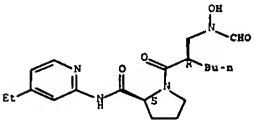
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 771478-82-1P 771478-84-3P 771478-85-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline N-formylhydroxylamine compds. for pharmaceuticals)
RN 771478-82-1 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-ethyl-2-pyridinyl)-, calcium salt (2:1) (9CI) (CA INDEX NAME)

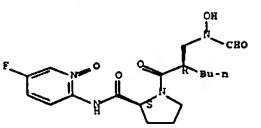
Absolute stereochemistry.



●1/2 Ca

RN 771478-84-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)-, zinc salt (2:1) (9CI) (CA INDEX NAME)

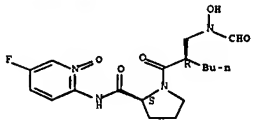
Absolute stereochemistry.



●1/2 Zn

RN 771478-85-4 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)-, calcium salt (2:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

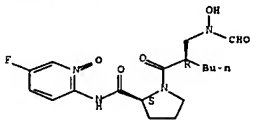


●1/2 Ca

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:846356 HCAPLUS Full-text
DOCUMENT NUMBER: 142:19798
TITLE: Antistaphylococcal activity of LBM415, a new peptide deformylase inhibitor, compared with those of other agents
AUTHOR(S): Credito, Kim; Lin, Gengrong; Ednie, Lois M.; Appelbaum, Peter C.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2004), 48(10), 4033-4036
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The MICs of LBM415, a new peptide diformylase inhibitor, were ≤0.06 to 4.0 μg/mL for 258 isolates of Staphylococcus aureus and coagulase-neg. staphylococci. LBM415 MICs were similar irresp. of whether the strains were methicillin susceptible or resistant. All strains were also susceptible to vancomycin, linezolid, ranbezolid, daptomycin, oritavancin, and quinupristin-dalfopristin. LBM415 at the MIC was bacteriostatic after 24 h.
IT 478913-91-6, LBM 415
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antistaphylococcal activity of LBM415, new peptide deformylase inhibitor, compared with those of other agents)
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:848355 HCAPLUS Full-text
DOCUMENT NUMBER: 142:3338
TITLE: Antipneumococcal activity of LBM415, a new peptide diformylase inhibitor, compared with those of other agents
AUTHOR(S): Ednie, Lois M.; Pankuch, Glenn; Appelbaum, Peter C.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2004), 48(10), 4027-4032
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

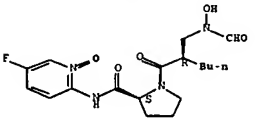
AB The MICs of LBM415, a new peptide diformylase inhibitor, were evaluated and ranged from 0.03 to 4.0 μg/mL for 300 pneumococci, irresp. of their β-lactam, macrolide, and quinolone susceptibilities. By comparison, vancomycin, teicoplanin, linezolid, and quinupristin-dalfopristin were also active, with MICs≤2.0 μg/mL. Gatifloxacin and moxifloxacin were the most active quinolones tested, while the MICs of the β-lactams rose with those of penicillin G. LBM415 at two times the MIC was bactericidal (99.9% killing) against six strains after 24 h.

IT 478913-91-6, LBM 415
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antipneumococcal activity of LBM415, new peptide diformylase inhibitor, compared with those of other agents)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

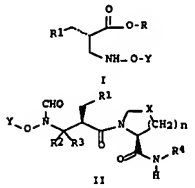


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:740215 HCAPLUS Full-text
DOCUMENT NUMBER: 141:261060
TITLE: Process for preparing β-amino acid intermediates in the synthesis of aminoacylpyrrolidinecarboxamides and related antibacterial compounds
INVENTOR(S): Prashad, Mahavir; Kim, Hang-yong; Hu, Bin; Slade, Joel; Kapa, Prasad Koteswara; Girgis, Michael John
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004076053	A2	20040910	WO 2004-US5159	20040220
WO 2004076053	A3	20041202		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004216178	A1	20040910	AU 2004-216178	20040220
CA 2516465	A1	20040910	CA 2004-2516465	20040220
EP 1599440	A2	20051130	EP 2004-713381	20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007448	A	20060131	BR 2004-7448	20040220
CN 1759097	A	20060412	CN 2004-80006326	20040220
JP 2006519786	T	20060831	JP 2006-503764	20040220
PRIORITY APPLN. INFO.:			US 2003-449015P P	20030221
			US 2003-449016P P	20030221
			US 2003-449017P P	20030221
			WO 2004-US5159 A	20040220

OTHER SOURCE(S): CASREACT 141:261060; MARPAT 141:261060
GI



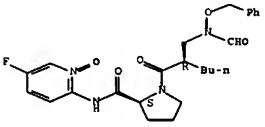
AB β-Amino acid derivs. I (R is alkyl, R1-R3 are H or alkyl or R2R3C are cycloalkyl, Y is a protecting group), intermediates in the synthesis of aminoacyl azacycloalkanes II [same R-R3 and Y, R4 is aryl or heteroaryl, n is 0-3, X is CH2, S, CHOH, CH(OR), CH(SH), CF2, C:N(OR) or CHF] were prepared by hydrogenation of corresponding α-alkylidene derivs. in the presence of a chiral ligand and a catalytic amount of a hydrogenation catalyst. Thus, a mixture of 2-[[(phenylmethoxy)amino]methyl]-2-hexenoic acid Me ester (.apprx. 1:1 E/Z, preparation given), bis(norbornadiene)rhodium(I) tetrafluoroborate and (1S,1'S,2R,2'R)-TangPhos in deoxygenated methanol in a Parr bottle is hydrogenated under H2 (45-55 psi) at room temperature for 24 h to afford 94 % 2- [[(phenylmethoxy)amino]methyl]-(2S)-hexanoic acid Me in 95 % yield (R:S = 98:2).

IT 478913-93-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of β-amino acid intermediates in synthesis of aminoacylpyrrolidinecarboxamides and related antibacterial compds.)

RN 478913-93-8 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

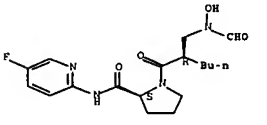


IT 478912-56-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of β-amino acid intermediates in synthesis of aminoacylpyrrolidinecarboxamides and related antibacterial compds.)

RN 478912-56-0 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:383872 HCAPLUS Full-text
DOCUMENT NUMBER: 141:170760
TITLE: Antimicrobial spectrum and activity of NVP PDF-713, a

novel peptide deformylase inhibitor, tested against 1,837 recent gram-positive clinical isolates
AUTHOR(S): Jones, Ronald N.; Fritsche, Thomas R.; Sader, Helio S.
CORPORATE SOURCE: The JONES Group/JMI Laboratories, North Liberty, IA, USA
SOURCE: Diagnostic Microbiology and Infectious Disease (2004), 49(1), 63-65
CODEN: DMIDDZ; ISSN: 0732-8893
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

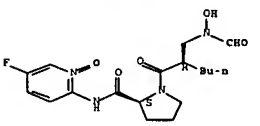
AB Continued emergence of antimicrobial resistances among gram-pos. pathogens requires further development of compds. with novel modes of action. The peptide deformylase inhibitor NVP PDF-713 was tested against 1,837 recent strains of Gram-pos. organisms. All NVP PDF-713 MICs were at ≤4μg/mL except for 6 enterococci (0.3% of strains overall). NVP PDF-713 MIC90 results were: Staphylococcus aureus, β-haemolytic and viridans group streptococci and Streptococcus bovis at 1 μg/mL; coagulase-neg. staphylococci, Streptococcus pneumoniae, and Listeria spp. at 2 μg/mL; and the enterococci at 4 μg/mL. NVP PDF-713 appears to be a promising new agent worthy of continued in vivo development.

IT 478913-91-6, NVP PDF-713
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic spectrum and activity of peptide deformylase inhibitor NVP PDF-713 gram-pos. pathogens)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:361959 HCAPLUS Full-text
DOCUMENT NUMBER: 141:136885
TITLE: Potential utility of a peptide deformylase inhibitor (NVP PDF-713) against oxazolidinone-resistant or streptogramin-resistant Gram-positive organism isolates
AUTHOR(S): Jones, Ronald N.; Moet, Gary J.; Sader, Helio S.; Fritsche, Thomas R.
CORPORATE SOURCE: The JONES Group/JMI Laboratories, North Liberty, IA, 52317, USA
SOURCE: Journal of Antimicrobial Chemotherapy (2004), 53(5), 804-807
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal

LANGUAGE: English

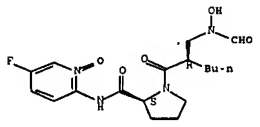
AB The potency of a novel peptide deformylase inhibitor, NVP PDF-713, was evaluated against Gram-pos. organisms having resistances to linezolid or quinupristin/dalfopristin. A total of 45 strains from three genera (six species groups) were tested by reference broth microdilution methods. The mechanism of resistance to the oxazolidinone was determined by sequencing of the gene encoding the ribosomal target. NVP PDF-713 retained activity against linezolid-resistant staphylococci (MIC range 0.25-2 mg/L), Streptococcus oralis (MIC 0.5 mg/L), Enterococcus faecalis (MIC range 2-4 mg/L) and Enterococcus faecium (MIC range 0.5-4 mg/L). Quinupristin/dalfopristin-resistant E. faecium (MIC range 1-2 mg/L) and staphylococci (MIC range 0.12-2 mg/L) were also inhibited by NVP PDF-713. Many (10 of 13 strains) of the linezolid-resistant enterococci were resistant to vancomycin and these clin. strains had a G2576U ribosomal target mutation. Thus, NVP PDF-713 appears to be a promising clin. candidate among the peptide deformylase inhibitors for the treatment of infections caused by Gram-pos. organisms that possess resistances to oxazolidinones or streptogramin combinations.

IT 478913-91-6, NVP PDF-713
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potential utility of peptide deformylase inhibitor NVP PDF-713 against oxazolidinone-resistant or streptogramin-resistant Gram-pos. organism isolates)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267293 HCAPLUS Full-text
DOCUMENT NUMBER: 140:287275
TITLE: Process for preparing benzyloxyaminoacylpyrrolidinecarboxamides
INVENTOR(S): Kapa, Prasad Koteswara; Jiang, Xinglong; Loeser, Eric M.; Slade, Joel; Prashad, Mahavir; Lee, George Tien-San
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026824	A1	20040401	WO 2003-EP10416	20030918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW

RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2499426	A1	20040401	CA 2003-2499426	20030918
AU 2003273404	A1	20040408	AU 2003-273404	20030918
EP 1542968	A1	20050622	EP 2003-755559	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014592	A	20050809	BR 2003-14592	20030918
CN 1684945	A	20051019	CN 2003-822471	20030918
JP 2006503053	T	20060126	JP 2004-537129	20030918
ZA 2005001923	A	20050912	ZA 2005-1923	20050307
IN 2005CN00346	A	20070406	IN 2005-CN346	20050308
NO 2005001867	A	20050418	NO 2005-1867	20050418
US 2005261504	A1	20051124	US 2005-527628	20050525
PRIORITY APPLN. INFO.:			US 2002-411920P P	20020919
			US 2003-480242P P	20030620
			WO 2003-EP10416 W	20030918

OTHER SOURCE(S): CASREACT 140:287275; MARPAT 140:287275

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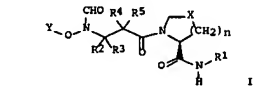

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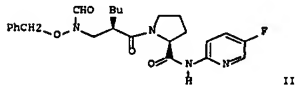


II

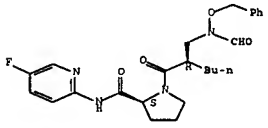
AB Title compds. I [Y = protective group; R1 = aryl, heteroaryl; R2-R5 = H, aliph; R2R3, R4R5 = alkylene; X = CH2, S, (un)substituted CH(OH), CH(SH), CF2, C:NOH, CHF; n = 0-3] were prepared for use as intermediates to prepare certain antibacterial N-formyl hydroxylamine compds. which are peptide deformylase inhibitors. Thus, HOCH2CHBuCO2H was treated with PhCH2ONH2, followed by MeSO2Cl to give MeSO3CH2CHBuCONHOCH2Ph, which was cyclized to the β-lactam and treated with (S)-N-(5-fluoro-2-pyridinyl)pyrrolidine- 2-carboxamide, followed by formylation to give the pyrrolidine II.

IT 478913-92-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparing benzyloxyaminoacylpyrrolidinecarboxamides)

RN 478913-92-7 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:94769 HCAPLUS Full-text
DOCUMENT NUMBER: 141:274236
TITLE: Disk diffusion quality control guidelines for NVP-PDF 713: a novel peptide deformylase inhibitor
AUTHOR(S): Anderegg, Tamara R.; Jones, Ronald N.
CORPORATE SOURCE: The Quality Control Working Group, The Jones Group/JMI Laboratories, North Liberty, IA, USA
SOURCE: Diagnostic Microbiology and Infectious Disease (2004), 48(1), 55-57
CODEN: DMIDDZ; ISSN: 0732-8893
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

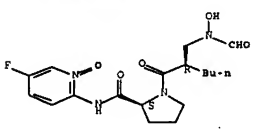
AB NVP-PDF713 is a peptide deformylase inhibitor that has emerged as a candidate for treating Gram-pos. infections and selected Gram-neg. species that commonly cause community-acquired respiratory tract infections. This report summarizes the results of a multi-center (seven participants) disk diffusion quality control (QC) investigation for NVP PDF-713 using guidelines of the National Committee for Clin. Laboratory Stds. and the standardized disk diffusion method. A total of 420 NVP-PDF 713 zone diameter values were generated for each QC organism. The proposed zone diameter ranges contained 97.6-99.8% of the reported participant results and were: Staphylococcus aureus ATCC 25923 (25-35 mm), Streptococcus pneumoniae ATCC 49619 (30-37 mm), and Haemophilus influenzae ATCC 49247 (24-32 mm). These QC criteria for the disk diffusion method should be applied during the NVP-PDF 713 clin. trials to maximize test accuracy.

IT 478913-91-6
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of peptide deformylase inhibitor NVP-PDF 713 against respiratory tract pathogens by disk diffusion testing)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:883789 HCAPLUS Full-text
DOCUMENT NUMBER: 141:20308
TITLE: Antibacterial susceptibility of a vancomycin-resistant Staphylococcus aureus strain isolated at the Hershey Medical Center
AUTHOR(S): Bozdogan, Buelent; Esel, Duygu; Whitener, Cynthia; Browne, Frederick A.; Appelbaum, Peter C.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Journal of Antimicrobial Chemotherapy (2003), 52(5), 864-868
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

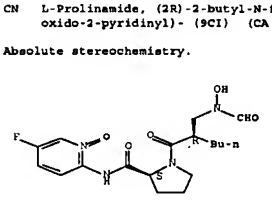
AB Staphylococcus aureus strain HMC3 isolated at the Hershey Medical Center, was resistant to vancomycin (VRSA) through the presence of the vanA resistance gene; it also contained mecA, erm(A), erm(B), tet(K) and aac(6')-aph(2''), conferring resistance to licensed β-lactams, macrolides, tetracycline and aminoglycosides. HMC3 also had alterations in GyrA and GrlB and was resistant to available quinolones. Exptl. drugs with low MICs (<2 mg/L) for VRSA HMC3 included cephalosporins BAL9141 and RWJ-54428; glycopeptides oritavancin and dalbavancin; the lipopeptide daptomycin; the glycolipodepsipeptide ramoplanin; new fluoroquinolones WCK 771 A, WCK 1153, DK-507k and sitafloxacin; and the DNA nanobinder GS02-02. These agents were all bactericidal as were trimethoprim/sulfamethoxazole and teicoplanin (MIC 4 mg/L). Oxazolidinones linezolid and ranbezolid; the injectable streptogramin quinupristin/dalfopristin; DNA nanobinders GS2-10547 and GS02-104; peptide deformylase inhibitors NVP-PDF713 and GS02-12; tetracycline derivative tigecycline; the antifolate iclaprim; mupirocin and fusidic acid were all active in vitro but bacteriostatic.

IT 478913-91-6
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibacterial susceptibility of a vancomycin-resistant Staphylococcus aureus strain isolated at the Hershey Medical Center)

RN 478913-91-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:977804 HCAPLUS Full-text

DOCUMENT NUMBER: 138:55863
TITLE: Preparation of N-formyl-N-hydroxylamino-substituted pyrrolidine derivatives as inhibitors of peptidyl deformylase
INVENTOR(S): Patel, Dinesh V.; Yuan, Zhengyu; Jain, Rakesh K.; Garcia Alvarez, Salvador; Jacobs, Jeffrey
PATENT ASSIGNEE(S): Versicor, Inc., USA; Novartis AG
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102790	A1	20021227	WO 2002-EP6604	20020614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2448526	A1	20021227	CA 2002-2448526	20020614
AU 2002321062	A1	20030102	AU 2002-321062	20020614
US 2003045479	A1	20030306	US 2002-171706	20020614
US 7148242	B2	20061212		
EP 1401828	A1	20040331	EP 2002-754681	20020614
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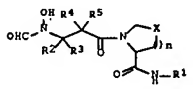
HU 200400208	A2	20040628	HU 2004-208	20020614
CN 1511152	A	20040707	CN 2002-810596	20020614
BR 2002010377	A	20040810	BR 2002-10377	20020614
JP 2005502606	T	20050127	JP 2003-506263	20020614
NZ 529489	A	20051028	NZ 2002-529489	20020614
AT 323081	T	20060415	AT 2002-754681	20020614
PT 1401828	T	20060831	PT 2002-754681	20020614
ES 2262824	T3	20061201	ES 2002-2754681	20020614
ZA 2003008379	A	20040521	ZA 2003-8379	20031028
IN 2003CN01963	A	20060106	IN 2003-CN1963	20031210
NO 2003005571	A	20040216	NO 2003-5571	20031212
HK 1064370	A1	20061020	HK 2004-107013	20040914

PRIORITY APPLN. INFO.:
US 2001-298419P P 20010615
US 2002-360313P P 20020227
WO 2002-EP6604 W 20020614

OTHER SOURCE(S): MARPAT 138:55863
GI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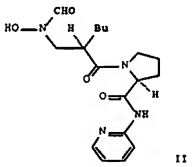
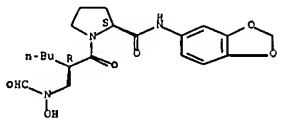

II

AB Title compds. I [X = CH2, S, CHOH, CH-alkoxy, CHSH, etc.; R1 = (hetero)aryl; R2-5 = H, alkyl, etc.; n = 0-3 provided that when n = 0, X = CH2] are prepared For instance, (S)-2-(chlorocarbonyl)pyrrolidine-1- carboxylic acid benzyl ester is used to acylate 2-aminopyridine and the resulting amide deprotected and coupled to (2R)-2-[(benzyloxyformylamino)methyl]hexanoic acid (preparation given; dioxane, HATU, i-Pr2NEt) to give II. IC50 of selected examples of I against MMP-7 ranges from >10 pM to >100 pM, whereas the IC50 of these same compds. against zinc-containing peptidyl deformylase (PDF) ranges from about 0.005 pM to 5 pM, and against nickel-containing PDF ranges from about 0.001 pM to about 0.3 pM. I are useful for preventing contamination of a cell culture medium.

IT 478913-80-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of N-formyl-N-hydroxylamino-substituted pyrrolidine derivs. as inhibitors of peptidyl deformylase)
RN 478913-80-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-1,3-benzodioxol-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

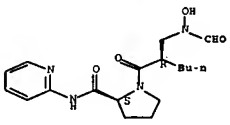


IT 478912-45-7P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(pyridin-2-yl)amide 478912-46-0P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-methylpyridin-2-yl)amide 478912-50-4P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(6-methylpyridin-2-yl)amide 478912-52-6P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-methylpyridin-2-yl)amide 478912-56-0P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-fluoropyridin-2-yl)amide 478912-59-3P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-methylpyridin-2-yl)amide 478912-63-9P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(6-ethylpyridin-2-yl)amide 478912-66-2P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-trifluoromethylpyridin-2-yl)amide 478912-69-5P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(6-fluoropyridin-2-yl)amide 478912-76-4P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4,6-dimethyl-1-oxopyridin-2-yl)amide 478912-80-0P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-methyl-1-oxopyridin-2-yl)amide 478912-85-5P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]azetidine-2-carboxylic acid N-(pyridin-2-yl)amide 478912-92-4P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-

carboxylic acid N-(4,6-dimethylpyridin-2-yl)amide 478912-97-9P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-ethylpyridin-2-yl)amide 478913-05-2P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-hydroxypyridin-2-yl)amide 478913-12-1P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(isoquinolin-1-yl)amide 478913-16-5P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(quinolin-3-yl)amide 478913-21-2P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]azetidine-2-carboxylic acid N-(4-methylpyridin-2-yl)amide 478913-24-5P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]azetidine-2-carboxylic acid N-(5-methylpyridin-2-yl)amide 478913-27-8P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]azetidine-2-carboxylic acid N-(5-fluoropyridin-2-yl)amide 478913-30-3P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-trifluoromethyl-1-oxopyridin-2-yl)amide 478913-37-0P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-phenylpyridin-2-yl)amide 478913-41-6P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-phenyl-1-oxopyridin-2-yl)amide 478913-45-0P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-trifluoromethylpyridin-2-yl)amide 478913-48-3P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-trifluoromethyl-1-oxopyridin-2-yl)amide 478913-51-8P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(8-hydroxyquinolin-2-yl)amide 478913-55-2P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-methoxy-6-methylpyridin-2-yl)amide 478913-59-6P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(4-methoxypyridin-2-yl)amide 478913-64-3P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-methoxypyridin-2-yl)amide 478913-68-7P, (2S)-1-[(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-methoxypyridin-2-yl)amide 478913-69-8P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(6-hydroxypyridin-2-yl)amide 478913-75-6P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-hydroxy-1-oxopyridin-2-yl)amide 478913-83-6P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(2,2-difluorobenzo[1,3]dioxol-5-yl)amide 478913-87-0P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(3-phenoxyphenyl)amide 478913-91-6P, (2S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-fluoro-1-oxopyridin-2-yl)amide 478913-94-9P 478913-96-1P, (2S,4R)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]-4-hydroxypyrrolidine-2-carboxylic acid N-(5-methylpyridine-2-yl)amide 478913-99-4P, (2S,4S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]-4-hydroxypyrrolidine-2-carboxylic acid N-(5-methylpyridine-2-yl)amide 478914-01-1P, (2S,4R)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]-4-hydroxypyrrolidine-2-carboxylic acid N-(4-ethylpyridine-2-yl)amide 478914-03-3P, (2S,4R)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]-4-hydroxypyrrolidine-2-carboxylic acid N-(5-trifluoromethylpyridine-2-yl)amide 478914-05-5P, (2S,4S)-4-Fluoro-1-[(2R)-2-[(formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-methylpyridine-2-yl)amide 478914-08-8P, (2S,4R)-4-Fluoro-1-[(2R)-2-[(formylhydroxyamino)methyl]hexanoyl]pyrrolidine-2-carboxylic acid N-(5-methylpyridine-2-yl)amide 478914-10-2P 478914-12-4P, (2S,4R)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]-4-methoxypyrrolidine-2-carboxylic acid N-(5-methylpyridin-2-yl)amide 478914-17-9P, (2S,4S)-1-[(2R)-2-[(Formylhydroxyamino)methyl]hexanoyl]-4-methoxypyrrolidine-2-carboxylic acid N-(5-methylpyridin-2-yl)amide

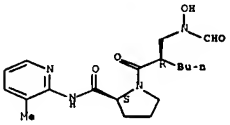
479067-88-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-formyl-N-hydroxylamino-substituted pyrrolidine derivs. as inhibitors of peptidyl deformylase)
RN 478912-45-7 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-2-pyridinyl- (CA INDEX NAME)

Absolute stereochemistry.



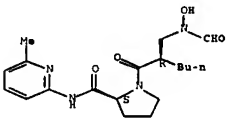
RN 478912-48-0 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(3-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 478912-50-4 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

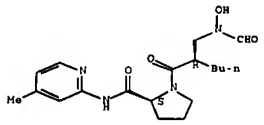
Absolute stereochemistry.



RN 478912-52-6 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

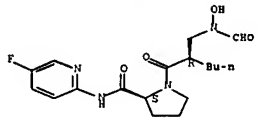
Absolute stereochemistry.



RN 478912-56-0 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

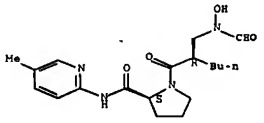
Absolute stereochemistry.



RN 478912-59-3 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

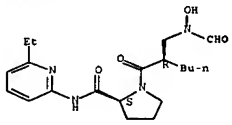
Absolute stereochemistry.



RN 478912-63-9 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(6-ethyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

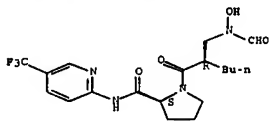
Absolute stereochemistry.



RN 478912-66-2 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-[5-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

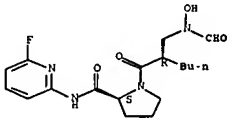
Absolute stereochemistry.



RN 478912-69-5 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(6-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

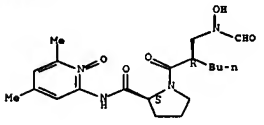
Absolute stereochemistry.



RN 478912-76-4 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4,6-dimethyl-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

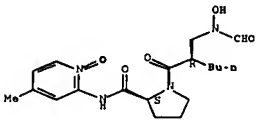
Absolute stereochemistry.



RN 478912-80-0 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-methyl-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

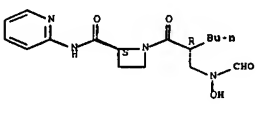
Absolute stereochemistry.



RN 478912-85-5 HCAPLUS

CN 2-Azetidinecarboxamide, 1-[(2R)-2-[(formylhydroxyamino)methyl]-1-oxohexyl]-N-2-pyridinyl-, (2S)- (9CI) (CA INDEX NAME)

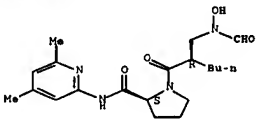
Absolute stereochemistry.



RN 478912-92-4 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4,6-dimethyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

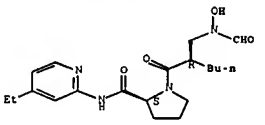
Absolute stereochemistry.



RN 478912-97-9 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-ethyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

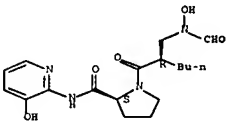
Absolute stereochemistry.



RN 478913-05-2 HCAPLUS

CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(3-hydroxy-2-pyridinyl)- (9CI) (CA INDEX NAME)

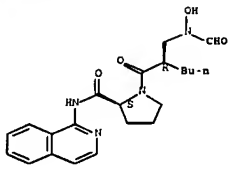
Absolute stereochemistry.



RN 478913-12-1 HCAPLUS

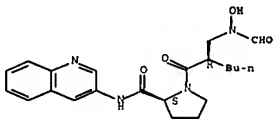
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-1-isoquinolinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



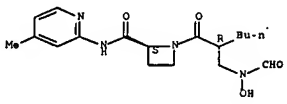
RN 478913-16-5 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-3-quinolinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



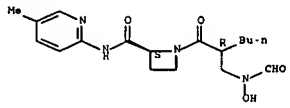
RN 478913-21-2 HCAPLUS
CN 2-Azetidinecarboxamide, 1-[(2R)-2-[(formylhydroxyamino)methyl]-1-oxohexyl]-N-(4-methyl-2-pyridinyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



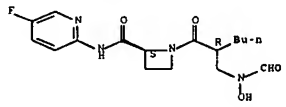
RN 478913-24-5 HCAPLUS
CN 2-Azetidinecarboxamide, 1-[(2R)-2-[(formylhydroxyamino)methyl]-1-oxohexyl]-N-(5-methyl-2-pyridinyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



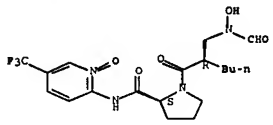
RN 478913-27-8 HCAPLUS
CN 2-Azetidinecarboxamide, N-(5-fluoro-2-pyridinyl)-1-[(2R)-2-[(formylhydroxyamino)methyl]-1-oxohexyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



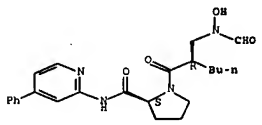
RN 478913-30-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-[1-oxido-5-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



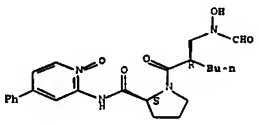
RN 478913-37-0 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-phenyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



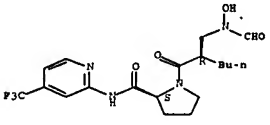
RN 478913-41-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(1-oxido-4-phenyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



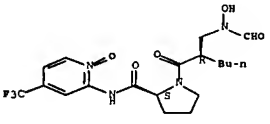
RN 478913-45-0 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-[4-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



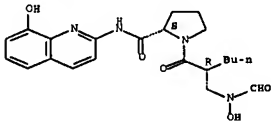
RN 478913-48-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-[1-oxido-4-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



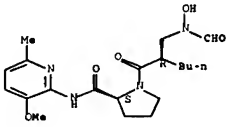
RN 478913-51-8 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(8-hydroxy-2-quinolinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



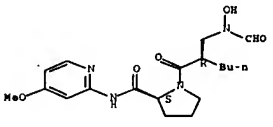
RN 478913-55-2 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(3-methoxy-6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



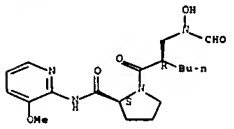
RN 478913-59-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-methoxy-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



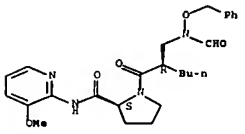
RN 478913-64-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(3-methoxy-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



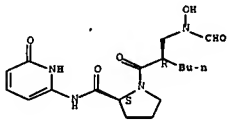
RN 478913-68-7 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(3-methoxy-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



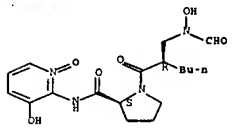
RN 478913-69-8 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(1,6-dihydro-6-oxo-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



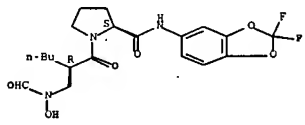
RN 478913-75-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(3-hydroxy-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



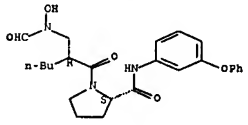
RN 478913-83-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(2,2-difluoro-1,3-benzodioxol-5-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



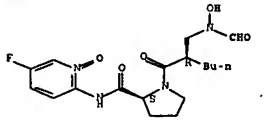
RN 478913-87-0 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(3-phenoxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



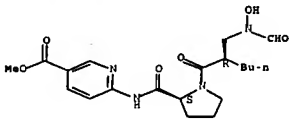
RN 478913-91-6 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



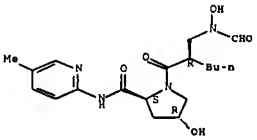
RN 478913-94-9 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-[5-(methoxycarbonyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



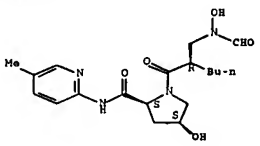
RN 478913-96-1 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-hydroxy-N-(5-methyl-2-pyridinyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



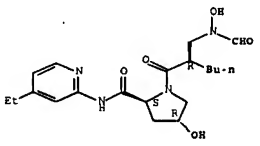
RN 478913-99-4 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-hydroxy-N-(5-methyl-2-pyridinyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



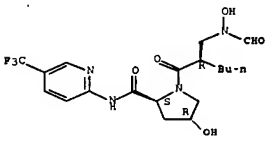
RN 478914-01-1 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-ethyl-2-pyridinyl)-4-hydroxy-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



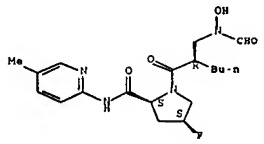
RN 478914-03-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-hydroxy-N-[5-(trifluoromethyl)-2-pyridinyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



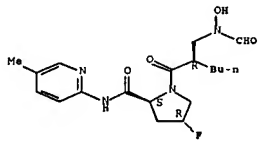
RN 478914-05-5 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-fluoro-N-(5-methyl-2-pyridinyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



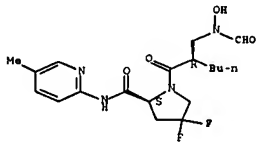
RN 478914-08-8 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-fluoro-N-(5-methyl-2-pyridinyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



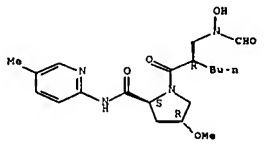
RN 478914-10-2 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4,4-difluoro-N-(5-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



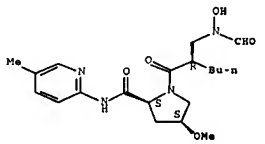
RN 478914-12-4 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-methoxy-N-(5-methyl-2-pyridinyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



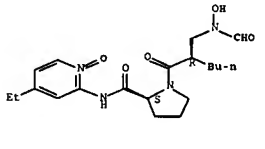
RN 478914-17-9 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-4-methoxy-N-(5-methyl-2-pyridinyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479067-88-4 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(4-ethyl-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

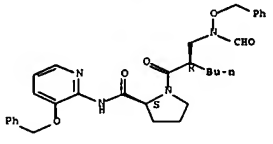
Absolute stereochemistry.



IT 478913-11-0P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(3-benzyloxypyridin-2-yl)amide
478913-15-4P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(isoquinolin-1-yl)amide
478913-20-1P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(quinolin-3-yl)amide
478913-63-2P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(4-methoxypyridin-2-yl)amide
478913-74-5P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(6-benzyloxypyridin-2-yl)amide
478913-79-0P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(3-benzyloxy-1-oxopyridin-2-yl)amide
478913-92-7P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(5-fluoropyridin-2-yl)amide
478913-93-8P, (2S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(5-fluoro-1-oxopyridin-2-yl)amide
478913-98-3P, (2S,4R)-4-(Benzyloxy)-1-{(2R)-2-{(formylhydroxyamino)methyl]hexanoyl}pyrrolidine-2-carboxylic acid N-(5-methylpyridine-2-yl)amide 478914-16-8P, (2S,4R)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}-4-methoxypyrrolidine-2-carboxylic acid N-(5-methylpyridin-2-yl)amide
478914-21-5P, (2S,4S)-1-{(2R)-2-[(Benzyloxyformylamino)methyl]hexanoyl}-4-methoxypyrrolidine-2-carboxylic acid N-(5-methylpyridin-2-yl)amide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-formyl-N-hydroxylamino-substituted pyrrolidine derive. as inhibitors of peptidyl deformylase)

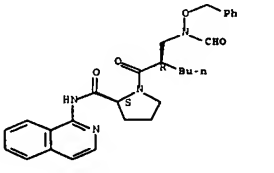
RN 478913-11-0 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-[3-(phenylmethoxy)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



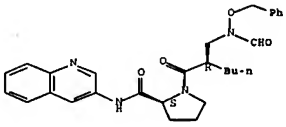
RN 478913-15-4 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-1-isoquinolinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



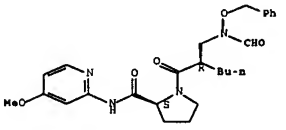
RN 478913-20-1 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-3-quinolinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



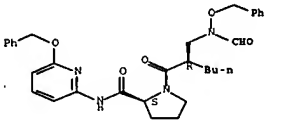
RN 478913-63-2 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(4-methoxy-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



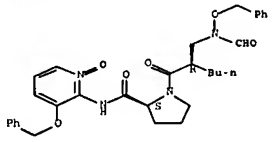
RN 478913-74-5 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-[6-(phenylmethoxy)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



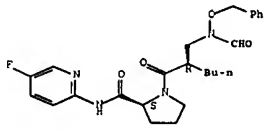
RN 478913-79-0 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-[1-oxido-3-(phenylmethoxy)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



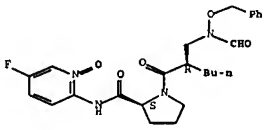
RN 478913-92-7 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



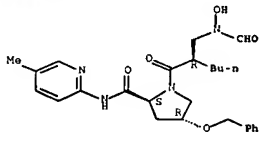
RN 478913-93-8 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-N-(5-fluoro-1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



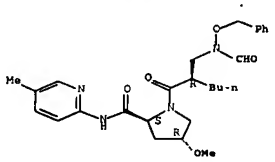
RN 478913-98-3 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-hydroxy-β-alanyl-N-(5-methyl-2-pyridinyl)-4-(phenylmethoxy)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



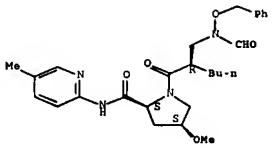
RN 478914-16-8 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-4-methoxy-N-(5-methyl-2-pyridinyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 478914-21-5 HCAPLUS
CN L-Prolinamide, (2R)-2-butyl-N-formyl-N-(phenylmethoxy)-β-alanyl-4-methoxy-N-(5-methyl-2-pyridinyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	173.84	760.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-24.96	-41.02

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 09:07:23 ON 30 MAY 2007